VOLUME XXVII FEBRUARY 1934 NUMBER 2

Southern Medical Journal

Journal of the Southern Medical Association

Published monthly by the Southern Medical Association, Empire Building, Birmingham, Ala. Annual subscription $4.00. Entered as Second-Class Matter at the Post Office at Birmingham, Ala., under act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Sec. 1103, Act of March 3, 1917, authorized Dec. 20, 1921.

Southern Medical Association, Twenty-Eighth Annual Meeting, San Antonio, Texas, November 13-16

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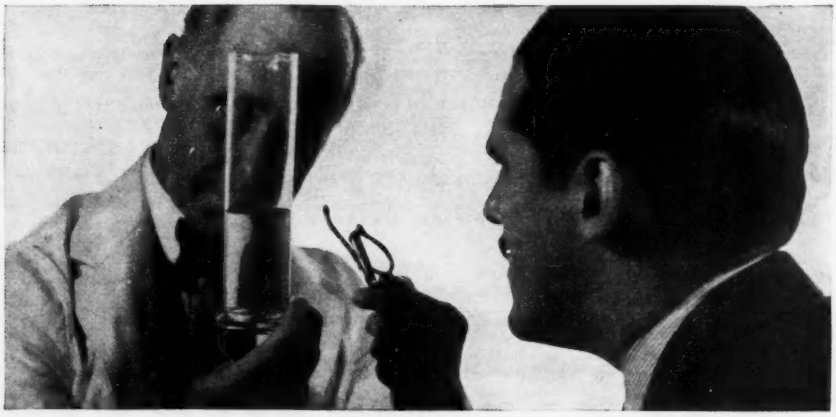

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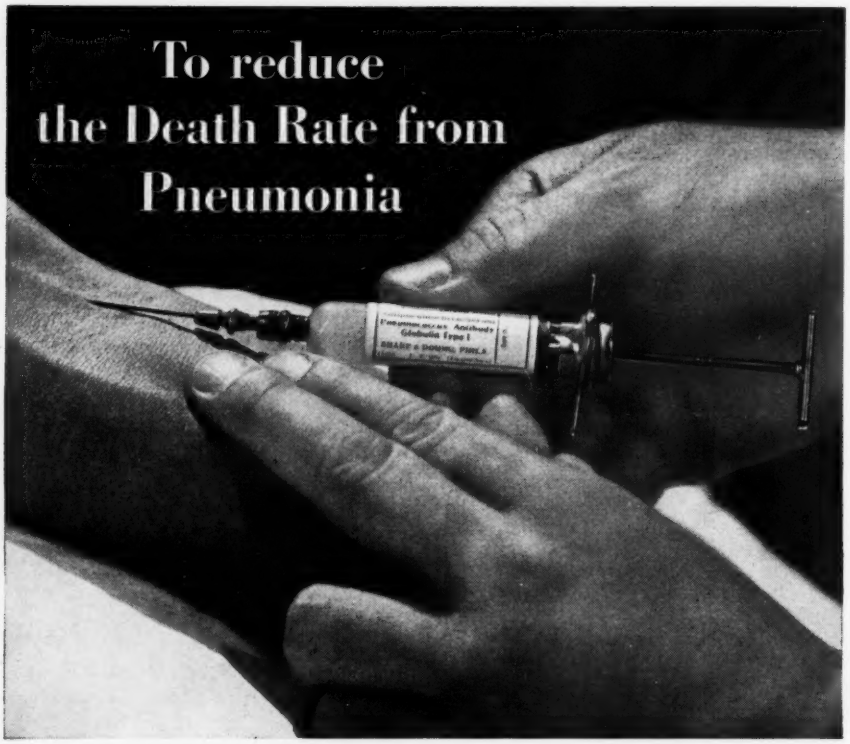

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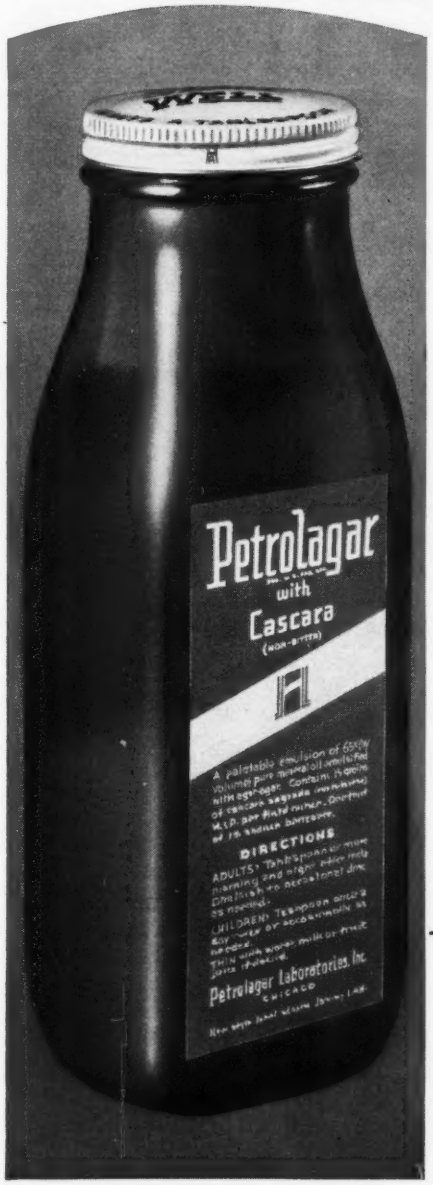

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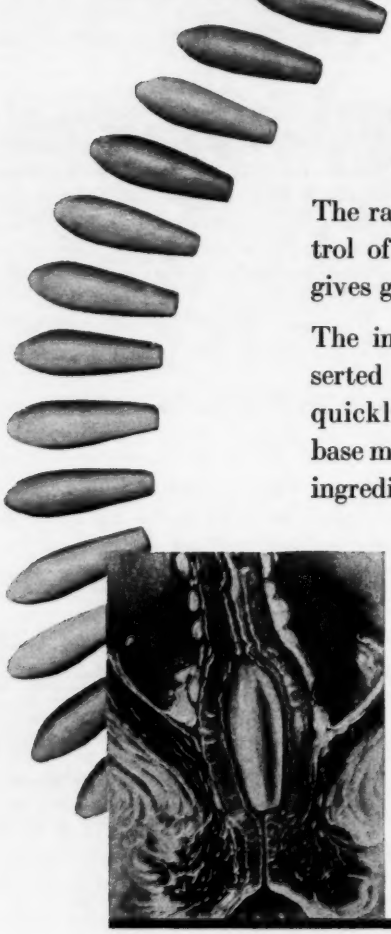

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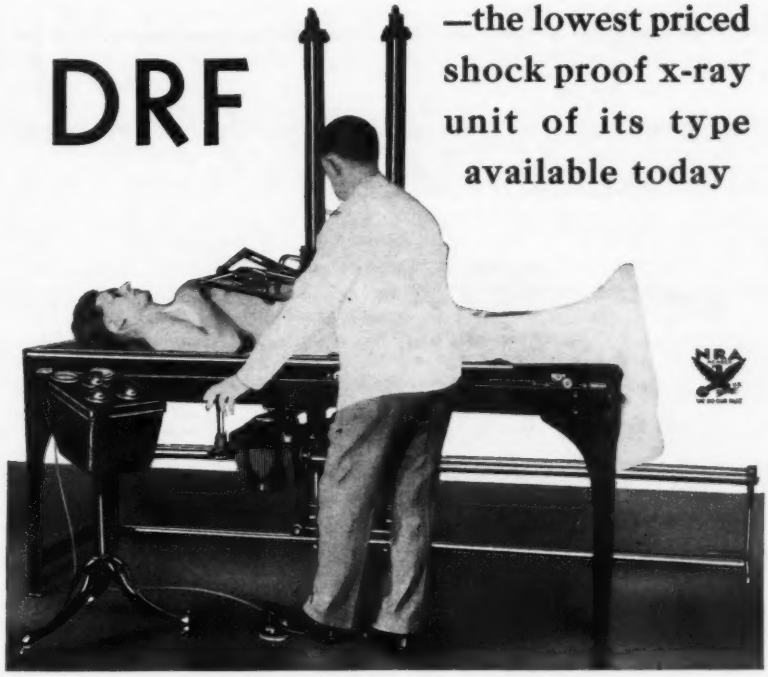

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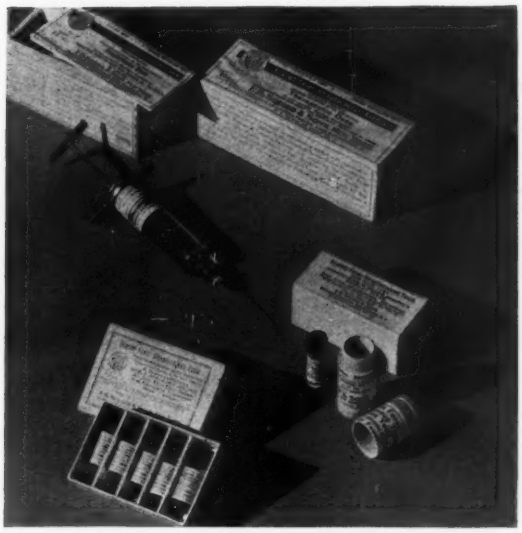

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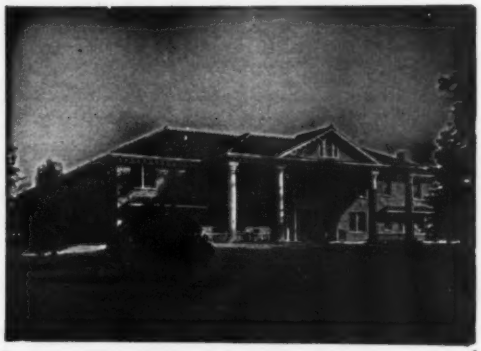

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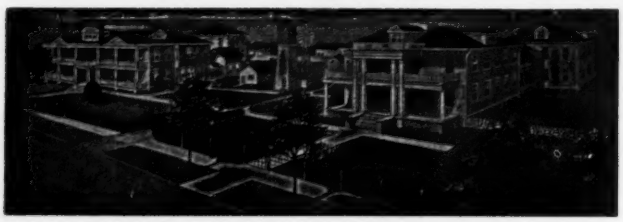

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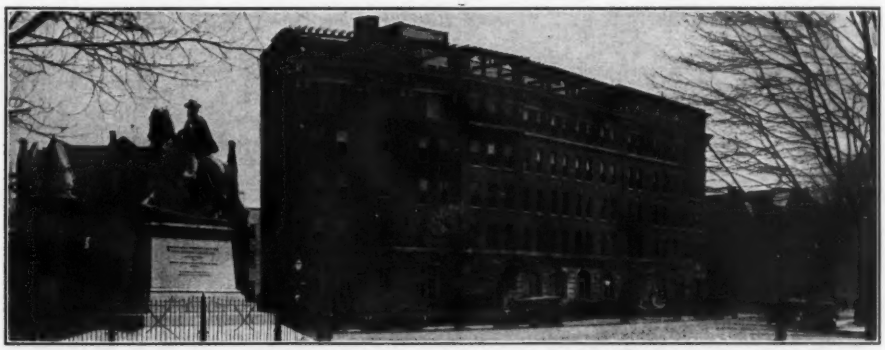

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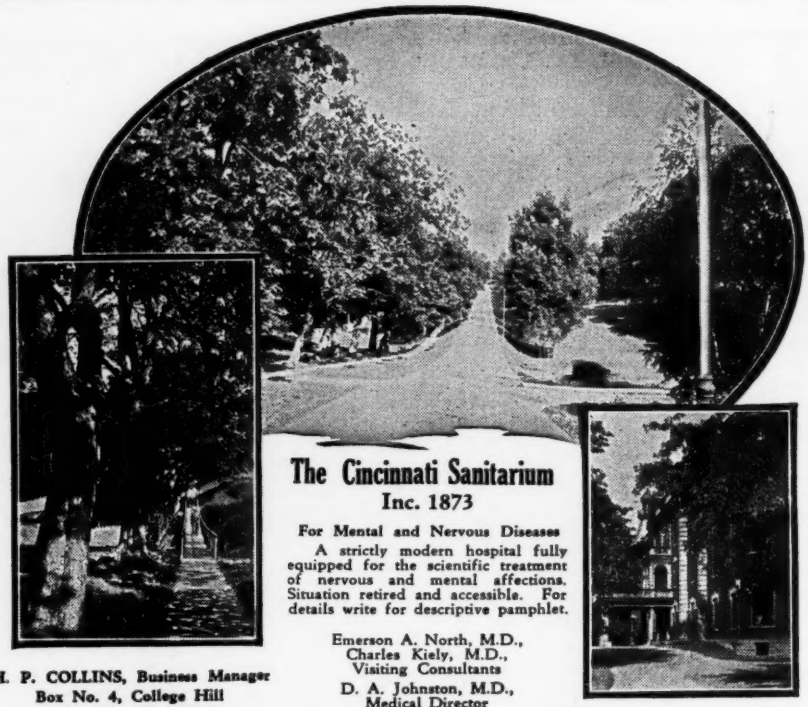

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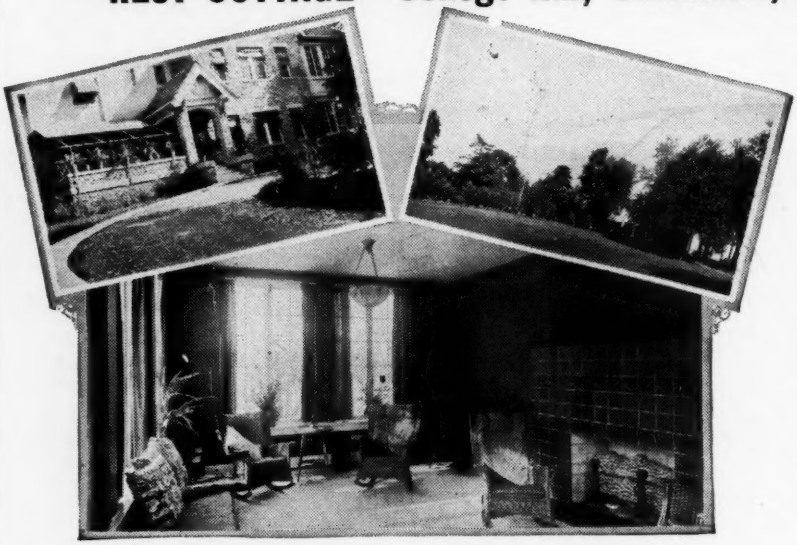

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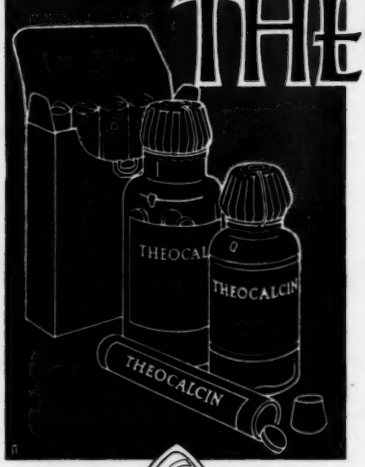

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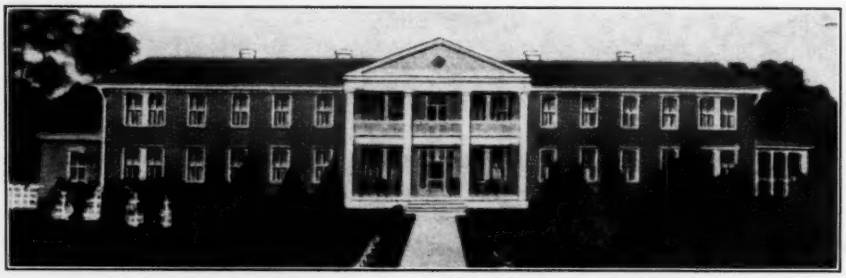

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JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

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Volume XXVII FEBRUARY 1934 Number 2

HIGH POINTS IN THIRTY-SIX YEARS OF RHINOLARYNGOLOGY*

By T. W. MOORE, M.D.,
Huntington, W. Va.

In 1897, when I began limiting my practice to diseases of the eye, ear, nose and throat, the relationship between the man who did this and the general practitioner was quite different from what it is today. Especially was this true in cases of such a disease as diphtheria, which was still a terrible scourge. Whilst the merits of antitoxin had been proven, it had been accepted by only a small proportion of the members of the medical profession. This is readily explained when we consider the method of administration. The maximum single dose was three thousand units, but usually only one thousand were given as the initial dose, this to be repeated every twelve hours, until there was an amelioration of symptoms. In fact, as late as 1901, an instructor[1] in laryngology in Cornell University said in his text-book:

"From one thousand to two thousand units should be employed, according to age and severity of symptoms, and the injection may be repeated in twelve hours. It is rarely necessary to exceed a total of six thousand units."

The average practitioner thought it was not necessary to administer antitoxin until other modes of treatment had failed. This usually carried us to the fourth or fifth day of the disease.

Welch,[2] in 1895, wrote a most convincing and comprehensive paper upon the treatment of diphtheria with antitoxin, a monograph giving the technic of administration of antitoxin, and a comparison of the prognosis with and without its use, which might be accepted as a text-book today, with only the modifications that improvement in manufacture of the product have rendered possible. The large dose may now be given in a small quantity of horse serum.

This paper fortunately I heard, and there was no question in my mind as to the efficacy of the treatment; but after several years' practice one of my confreres came to me and said:

"I have kept a record of the cases of diphtheria in which you have given antitoxin and those in which it has not been administered for the past two years, and I find the mortality is just as high where you gave it as where another treatment was used."

O'Dwyer perfected his intubation set and it was approved by a committee from the American Medical Association[3] in 1886, but the procedure was not generally accepted. When I began practice, in my town only one child had been intubated and it had died. During my first winter, there was an epidemic of the laryngeal type of diphtheria and I performed numerous intubations.[4] They were always done in homes, as we had no hospitals. Looking backward, the large percentage of recoveries is surprising.

Lennox Browne[5] was still advocating the removal of tonsils if they were large, and clipping the uvula if it was edematous, as therapeutic measures in acute diphtheria. He said that he had practiced this method for twenty years. In the fifth edition of his "Throat and Nose Diseases," published in 1899, he said:

"It is now twenty years since I first proposed and adopted the removal of enlarged tonsils and edematous uvulae during the acute stage of diphtheria. . . . I was quite prepared to hear the wisdom of this practice questioned; but however startling the procedure may at first sight appear, any objections which could be raised against it are theoretical rather than practical, and of no account in the balance, when weighed against its advantages."

The development of local anesthesia has been one of the greatest aids in our work. Of course, prior to 1897, cocaine was used as a local anesthetic, but the development of nerve blocking and infiltration anesthesia, especially when used in conjunction with the epinephrine products, has extended the scope and lessened the hazards

*Read in Section on Ophthalmology and Otolaryngology, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

of our operative work tremendously. I began employing the epinephrine products in 1897, using at first a solution made in my office from the powdered desiccated gland.

Intranasal surgery, in the beginning of my practice, was much more limited in its scope than it is today. Septal spurs were sawed off, with no attempt to conserve the mucous membrane; and for a more radical procedure the Asch operation, so called because Morris Asch[6] had perfected and described instruments for its performance, was employed. There were several modifications of this method of correcting septal deformities, none of which was satisfactory in more than a few conditions. These procedures, however, led to operations on the turbinates, and in 1902 the slaughter of these bodies, especially of the inferior turbinates, was rampant. In that year, at the meeting of one of our special national societies for eye, ear, nose and throat diseases, a writer[7] described a saw designed for this purpose and mentioned having performed the operation two hundred and sixty-four times on one hundred and fifty-five patients. In discussing this paper the president of the organization, a man who was later accorded the highest honors possible in nearly all our special societies, stated that he had operated upon between three and four thousand cases in private practice.

The benefits recorded by the majority of speakers make us hesitate today because we have no measures that are so universally satisfactory as theirs. From the literature, recurring attacks of otitis media catarrhalis acuta were absolutely and it seems to me always cured by removing a portion of the inferior turbinate.

At the meeting of the same organization[8] in 1904, a professor of otolaryngology exhibited a pie plate full of inferior turbinates that he had removed, and cited among the many advantages of this operation that it was unnecessary to remove adenoids where this turbinectomy was performed, as they would atrophy and disappear.

This surgery was advocated by numerous continental writers, especially in Germany, where Rindfleisch,[9] in an article in 1905, reported six hundred and twenty-seven conchotomies. But most of the papers that I have found advocating turbinectomy were from the Ohio Valley. One distinguished author stated that in this locality when the turbinates were removed they returned. I have often been impressed with the fact that the discomforts which, with our present knowledge, we are led to anticipate from this mutilating operation, were seldom seen.

In 1905, papers were being read describing the submucous resection of the septum, and Ballenger[10] presented his swivel knife. This operation was widely accepted in this country, with much ingenious instrumentation, so much so that Freer,[11] in his Chairman's Address before the Laryngological Section of the American Medical Association, felt called upon to denounce the "primitive and crude methods" being employed as well as

> "the blunt or chisel-edged elevators which transformed it from its true nature of an operation of deftness, neatness and painstaking deliberate skill into one whose aim is to finish the work quickly at the expense of thoroughness and with the use of a certain amount of blind force."

At the Triological meeting in 1905, Jackson[12] exhibited a bronchoscope, an esophagoscope, a tracheoscope, a laryngo-pharyngeal speculum, and a large forceps for use with them. This stimulated the interest in bronchoscopy and esophagoscopy, which rapidly gained momentum, particularly after Killian[13] appeared before the same organization in 1907.

Jackson has worked unceasingly with this branch of our specialty and is continually giving us something new. Before the Laryngological Section of the American Medical Association in June this year, he demonstrated most interestingly how foreign bodies in the esophagus may be the cause of pulmonary disease. The original design of the tubes used and their method of illumination as first suggested by him have undergone only slight modifications and are in use by the majority of specialists in this work in this country. They have been introduced all over the world.

The Bruenning tubes were shortly after this time modified by Kahler and in this form were used by many of the operators of Europe. During the last decade Haslinger, who is also a mechanical genius, has introduced a new method of reflecting the light into the tube which is a decided improvement over the other forms of distal illumination. His directoscope is most useful, and has superseded suspension laryngoscopy in much of our work.

These procedures, which at first were largely methods of removing foreign bodies, are now among our most useful diagnostic, surgical and medical aids.

Mosher,[14] in 1906, presented a paper on the esophagus. The year before, he had demonstrated the Killian method of inspecting the

trachea and esophagus. This paper was on the upper end of the esophagus. Showing his characteristic persistence and thoroughness, his Chairman's Address this year before the Laryngological Section of the American Medical Association was upon the same subject, but he has now, after many papers, and many years, reached the gastric end. As we all know, his studies have completely revised our knowledge of the anatomy and pathology of the gullet.

In 1901, Sir William Hunter wrote a monograph on focal infection with special reference to the teeth. He visited this country in 1910, aroused the dental profession to a consciousness of this condition and emphasized the fact that many capped and filled teeth had been preserved to the detriment of the patient's general health.

In 1911, dining one night in Dresden with an internist, I was informed that physicians there were curing rheumatic conditions by removing tonsils. The following morning I was taken to see Dr. Mann operate. He did a beautiful tonsillectomy under local anesthesia. He showed me patients in whom the results were most gratifying and I was convinced that this was truly a remedial measure. By this time laryngologists were decided that tonsillectomy was the operation that must be performed, so when Billings'[15] booklet appeared in 1916, we were ripe for the condemnation and removal of tonsils for many ills. This probably has done as much good as any radical procedure that has been generally adopted by the medical profession as a whole.

The sinuses had long been known as cavities that might and often did harbor infection. Caldwell[16] and Luc[17] had, prior to 1897, separately described the operation that bears their names, but many rhinologists were still entering the maxillary antrum through the socket of an extracted tooth, which, as you know, is always an awful mess.

Many operations on the sinuses have been described, had their vogue and passed out of our routine.

It has seemed to me that the operative procedure in pan-sinusitis that has contributed most to the help of the patient is the one carefully described and popularized by the frequent writing on its benefits by our beloved Lynch,[18] which is now usually described under his name.

Killian, in 1902,[19] Denker, in 1905,[20] Lothrop, in 1915,[21] and last year Ferris Smith, described methods that have distinctive features and have developed a more or less lasting following.

The idea that the nasal accessory sinuses may be the source of infection in the lungs and other organs has been developed during my time of work in this specialty. It has been with interest that I have followed the work of Mullin[22] and others. Their studies show the transmission of poison from these cavities through the lymphatic system. The results of these infections have been studied by Dean,[23] Marriott and numerous others. I never was able to endorse the radical operative treatment of the sinuses in children which was popular a few years ago, and am delighted that a more conservative routine again prevails.

Of course, before 1897 there were operators who washed the sinuses, maxillary, frontal and sphenoidal, through their natural openings, but today it is striking what a large percentage of maxillary and sphenoid sinuses can be and are being treated in this manner by the younger men.

A very valuable contribution that is today I think proven is that a person with an infected sinus may transmit the infection to another person. This probably explains why we often see a number of the members of a family thus afflicted.

In 1914, West presented a paper before the International Clinical Congress in London and demonstrated his method of performing his intranasal tear sac operation. This has since been modified by Koffler. It has, I think, proven a distinct advance in the treatment of dacryocystitis, is not difficult to perform and after five years' trial it is to me the most satisfactory.

Toti described his dacryocystectomy in 1909. This was modified by Mosher in 1922 and has been popular with many rhinologists.

I have watched the tremendous growth of serum and intravenous therapy of this century. Fostered by the manufacturing pharmacist, it has been overdone, and has afforded a great opportunity for exploitation of the patient by the less informed, or less conscientious practitioner, not so much probably in our specialty as in that of the man doing general work.

In my earlier years of practice we relied wholly upon the history, clinical findings and "therapeutic tests" for a diagnosis of syphilis. When definite blood tests were proven to be dependable much had been accomplished. I

doubt very much that the younger members of our group appreciate how much. To demonstrate, I will take an example from ophthalmology. In 1898, Sir Sidney Stephenson,[24] writing about iritis, said:

"Syphilis is, without doubt, the most common predisposing cause of iritis. Most authors credit the venereal disorder with 50 per cent of all cases, but that estimate is too low, especially if hereditary syphilis be taken into account. The proportion probably lies near 60 per cent."

One author, in 1931, said syphilis was the cause in only 4 per cent. I believe that most authors today think that about 19 per cent of the cases of iritis are due to the *Spirocheta pallida*.

I have seen the development of the x-ray and its application to our work, the introduction of spinal puncture, as well as blood tests for diagnosis, also blood transfusions, other intravenous injections, foreign protein and spinal therapy. Today it would be difficult for an up-to-date rhinologist or laryngologist to do his work without a laboratory as a constant adjunct. Particularly do we appreciate this in dealing with what to me is a constant maze of contradiction, known as allergy. It seems to me that our two most constant points in diagnosing this condition in the nose are the history and the eosinophils in the nasal secretion. In sinus allergy we find the roentgen pictures not dependable, for as you know we may have a film in the morning that would indicate pus in an antrum and in the afternoon another one that may be clear. We may have in some cases a dermal reaction to certain foods or inhaled substances and find the patient insensitive to these same things within a week or ten days. Hansel,[25] in a recent article, says:

"Upon the performance of skin tests in the diagnosis of allergy too much reliance should not be placed. A positive reaction represents nothing more than a clue."

However, the skin tests have certainly rewritten the chapter on hay-fever and asthma, and further we have learned that allergic conditions are not benefited by surgery *per se* and that operation is only beneficial where there is an infection or obstruction that demands this treatment, irrespective of the allergic condition.

We have learned that malignancy of the larynx can be cured only by early and thorough surgery coupled when needed with radiation, as in other regions of the body; and further that a chronic hoarseness, or frequently recurring attacks of hoarseness, demand our most careful and painstaking search for a beginning neoplasm which must be taken care of without delay.

In my early days in this work tuberculosis was very prevalent in the vicinity of my practice. I saw many cases of tuberculosis of the larynx. Fortunately today we see very few. Even then we were taught that the treatment was constitutional and that local treatment was only for the relief of pain. The advantages of rest were then recommended, but not the complete rest of the larynx advocated today, in which the patient communicates with his fellows by means of a writing pad. I have watched the development of the application of the actual cautery as a therapeutic measure in this disease with much interest and am convinced of its great value in many cases if it is properly applied.

With the work which is being done in the study of food reactions and body chemistry I am sure much good will ultimately result and undoubtedly much has been accomplished up to this time. But I cannot refrain from smiling when I think of the consternation that would have been manifested when I began this work had I told some of my clinical friends that I could prescribe a proper diet by looking into a patient's nose and determining the color of the mucous membrane of the septum.

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DISCUSSION (*Abstract*)

Dr. Dunbar Roy, Atlanta, Ga.—Dr. Moore's paper was especially interesting to me because I am one of the few members present today who is familiar with those remarkable changes in the practice of our specialty which he has enumerated. The paper is valuable as showing to the younger members of our Section the difficulties which the older men encountered in the practice of medicine and surgery. Surely the span of life must be lengthened if the same rate of progress in the management of physical ailments continues in the future which has been exemplified in the past.

Dr. Homer Dupuy, New Orleans, La.—Dr. Moore, in his extraordinary and large experience, referred to his brilliant results in intubation for acute laryngeal stenosis in children. It is yet my procedure of choice. With the administration of large doses of antidiphtheritic serum for such affections intubation is fast becoming a lost art. Both it and tracheotomy should be unnecessary; for a child with croupy cough, fever, dysphonia, dyspnea, in ninety-five cases out of a hundred has laryngeal diphtheria. I refer to the primary types, in which there is no faucial invasion with the local clinical signs which assist in diagnosis. Intubation is an art requiring the most delicate technic both in introducing and removing the tube. Unless one is specially trained, as Dr. Moore is, tracheotomy should be the procedure of choice. It is true that intubation reduces the incidence of pneumonia. It is a bloodless procedure. But its proper application requires great skill and judgment.

Dr. Clifton M. Miller, Richmond, Va.—The laboratory development to which Dr. Moore has called attention is certainly one of the most important in our special line of work as well as in every other line. In my mind, this enormous stride forward has not been without drawbacks. The main drawback seems to me to be the loss of the clinical sense of the individual physician. He is a better physician on account of the laboratory, but his judgment leans too much upon this. Again, we seem to have become too greatly specialized along certain lines and to have forgotten the great essential, that we must first be good physicians, then develop ourselves along any line that makes the greatest appeal. There seems to be now a great swinging of the pendulum in the direction of being good physicians and this is a very hopeful sign.

The discovery of insulin has been a boon to medicine. The development and knowledge of endocrinology has begun and this, with biochemistry, holds out brilliant prospects for the future in all medical lines.

Electricity was no new thing in 1897, but the development of its many medical uses has come since that time. Diathermy, with its many possibilities, and the infra-red and ultraviolet lights are now a part of our regular armamentarium. All forms of physiotherapy have their uses in our work as well as in that of the internist and surgeon.

We have made many advances, but our knowledge is far from complete. The men of this Section, particularly the younger ones, have a great opportunity for advancing the profession.

Dr. Moore (closing).—I consider intubation still a useful procedure in many cases and believe that it has a place in our work. Especially is this true in my community, but I might add that one of my sons, after serving four years in Bellevue Hospital, New York, says that during that time he did not see a single intubation.

NEPHRITIS AND PREGNANCY*

By H. J. STANDER, M.D.,
and
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In two recent papers[1] [2] we endeavored to evaluate the grave prognosis in chronic nephritis complicated by pregnancy, and stated that the average maternal mortality occurring within ten years in women suffering from this complication was approximately 40 per cent. It was, and still is, our belief that the strain of pregnancy on kidney function greatly aggravates an underlying chronic nephritis and thereby materially shortens the life of the individual. We advocated termination of pregnancy and prevention of any further pregnancies in a woman suffering from a definite and proven chronic nephritis.

The purpose of the present paper is to present a review of the patients with chronic nephritis treated in the obstetrical division of the Woman's Clinic of the New York Hospital during the twelve months ending September 1, 1933, to emphasize the value of certain kidney function tests in differential diagnosis and to put forth in detail our views as to treatment.

STATISTICS

OBSTETRICAL INDOOR SERVICE

September 1, 1932-August 31, 1933

Total patients discharged	3020
Total patients treated for a toxemia	472

Total incidence of toxemia of pregnancy, 15.6 per cent.

*Read in Section on Obstetrics, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

*From the Department of Obstetrics and Gynecology, New York Hospital and Cornell Medical College, New York.

Considering only delivered patients, we find that of the 363 patients discharged after delivery there were 64 cases of chronic nephritis, an incidence of 17.6 per cent in the total number of toxemia patients. The relative incidence is shown in *Table 1*. There were 20 other toxemia

Table 1

TYPE OF TOXEMIA OF PREGNANCY IN 363 CASES

Type of Toxemia	No. Cases	Percentage of Total Toxemias
Low reserve kidney	221	60.9
Chronic nephritis	64	17.6
Unclassified	36	9.9
Pre-eclampsia	28	7.7
Eclampsia	9	2.5
Vomiting of pregnancy	5	1.4
Total	363	100.

patients admitted as non-pregnant, comprising one of low reserve kidney, 15 of chronic nephritis and 4 unclassified.

A study of 74 chronic nephritis patients showed:

RACE

White	55
Colored	19

AGE

16 to 20 years	5
21 to 25 years	16
26 to 30 years	22
31 to 35 years	16
36 to 40 years	10
41 to 45 years	5

PRENATAL CARE

Good (3 or more visits)	46
Defective	10
None	3

WASSERMANN

Positive (treatment unknown)	1
Negative	65
Unknown	8

OTHER COMPLICATING DISEASES

Cardiac disease	5
Secondary anemia	1
Rheumatism	1

PREVIOUS TOXEMIA

Eclampsia	4
Type unknown	9
Vomiting of Pregnancy	3

PARITY

Gravida 0	1
1	22
2	13
3	11
4	4
5	4
6	2
7	5
8	3
9	4
10	1
11	0
12	3
13	1

Fourteen patients had admissions to the Hospital and were discharged during the antenatal period.

TYPE OF DELIVERY

Spontaneous	33=67.3 per cent
Operative	16=32.7 per cent
Forceps	3
Bougie induction	6
Breech extraction	3
Classical cesarean section	2
Classical cesarean section + sterilization	2
Abortion, therapeutic	4
Abortion, spontaneous	1

MORTALITY

Maternal	0
Infantile (not including abortions)	4=8.0 per cent

These infantile deaths are as follows:

(a) Stillborn macerated premature 1150 grams.
(b) Stillborn macerated premature 1880 grams.
(c) Stillborn, cellulitis of cord and septicemia.
(d) Died 2 hours after birth, partial atelectasis, extra dural hemorrhage of spinal cord.

All other infants were discharged in good condition. Eight had weighed less than 2,500 grams at birth. There was 1 set of twins.

Dispensary visits previous to delivery ranged from 1 to 18.

Blood pressure was 140/90 or above in 26 patients at the time of the first dispensary visit.

Elevation of blood pressure occurred in the first half of pregnancy in 13 patients.

ALBUMIN

Twenty-three patients showed no albumin. In others, the amount varied from a trace to 2 grams.

EYE EXAMINATION (45 CASES)

	Pregnant	Not Pregnant
Normal	14	2
Unknown	12	9
Arteriosclerosis	2	2
Hypertensive retinitis	2	
Tortuosity of arteries	1	
Haziness of disc		1

The average results for the three kidney function tests (urea clearance, phenolsulphonephthalein and creatinine) in 45 patients suffering from nephritis are shown in *Table 2*. These tests were conducted according to our earlier detailed description.[2]

Table 2

KIDNEY FUNCTION TESTS

Average Results on 45 Chronic Nephritic Patients

Test	Normal or Non-Nephritic	Nephritic Undelivered	Nephritic Delivered	Not Pregnant
Urea Clearance				
First	80 to 120	66.8	70.6	91.6
Second	80 to 120	64.2	65.6	86.4
Average	80 to 120	65.5	68.1	89.0
Phthalein total in 2 hours	80	67.9	73.4	71.6
Creatinine				
First hr.	50	55.9	51.1	67.3
Second hr.	180	126.6	141.5	139.9
Third hr.	100	114.1	99.3	105.1

The real difficulty in this type of toxemia of pregnancy is to know conclusively whether the patient has or has not an underlying nephritis. Once we have absolute proof of the presence of a nephritis, the problem is immensely simplified as to treatment, as will be shown later in this paper. It is our belief that one of the greatest problems today in the toxemias of pregnancy is the definite recognition of nephritis and that it is equaled in importance only by the problem of the etiology of eclampsia. This belief is based upon the experience that nephritis complicating pregnancy is more common than eclampsia, that nephritis is often not recognized and that the maternal mortality, both immediate and remote, is far higher than is commonly believed and taught. At present we[1] [2] consider nephritis complicated by pregnancy to be as serious as eclampsia. This is not the common belief, for the reason that the deaths in eclampsia are seen at the time of the attack, while the majority of the deaths from nephritis complicated by pregnancy occur after the patient has been discharged from the maternity hospital, or by her physician at the end of the puerperium. These deaths, if not during or immediately following pregnancy, usually occur from a few months to ten years following delivery, either in the same hospital but on the medical service, or in another hospital and often even in another community. It is only by a conscientious follow-up of our patients, over a period of years, that we can come to a true evaluation of the end-results in nephritis complicated by pregnancy.

We cannot agree with Goodall[3] that nephritis complicated by pregnancy is the same pathologic process as in pre-eclampsia, but under a different form of intensity, nor do our figures show that the cases in which it is possible to diagnose a nephritis antedating the pregnancy are relatively rare. We regard nephritis complicated by pregnancy as a distinct and separate entity, or disease process, from eclampsia and pre-eclampsia. The blood chemical findings,[4] the subsequent history of the patient[5] and the kidney function tests[6] all support this contention. We have seen no patient, in whom the diagnosis of nephritis complicated by pregnancy was established beyond doubt by clinical and laboratory findings, including repeated kidney function tests, who was "cured" of the nephritis during, or after, or by a pregnancy.

In an earlier study Stander and Peckham[1] presented the complete histories of a series of patients suffering from nephritis and observed during one to seven pregnancies. The history of one of these patients is recalled here, and it will be seen that during her second and third pregnancies, covering a period of five years, one would have been tempted to conclude that her first pregnancy cured her nephritis. We had innumerable observations on this patient, as shown in *Fig. 1*, proving beyond doubt that the nephritis was present in the first pregnancy in 1917, that for the five years she appeared to be cured and that from that time on her nephritis progressed and she died eight years later in nephritic uremia. Even after her fourth pregnancy there was a period of presumable arrest. A study of her chart (*Fig. 1*) shows the downhill course of the nephritis from the time of her first pregnancy in 1917 until her death in 1930, although a casual study of her condition during the years 1918 to 1922 may lead one to the erroneous conclusion that the nephritis was cured. Her duration of life after the first appearance of positive evidence of the presence of nephritis, in 1917, was twelve and one-half years, which is longer than the average for our nephritic patients, but this does not mean that the pregnancies alleviated the nephritis, but rather that without the pregnancies her duration of life might have been greatly prolonged. This chart (*Fig. 1*), as well as several others published in the original paper of Stander and Peckham, show how in certain cases one may easily, but erroneously, conclude that the patient does not have an underlying nephritis, or that the nephritis is cured during or by a pregnancy, should one study the patient during only one or two pregnancies and not over a period of five to ten years.

During the past month we have seen a patient admitted to the medical department of our hospital with all the signs and symptoms of the last stages of nephritis, having a nitrogenous retention amounting to 150 mg. of nonprotein nitrogen and now almost in uremia, who was told by her physician less than a year ago that her pregnancy would "cure" her nephritis. Furthermore, this patient is not in a class by herself, as we have seen other patients, dying from nephritis in from one to ten years following a pregnancy, in whom this same type of history was elicited. Such teaching we consider dangerous. It is true that there are certain patients in whom we suspect nephritis and in whom the condition may eventually clear up completely; but this proves that our diagnosis was probably wrong rather than that an underlying nephritis was cured by a pregnancy. We repeat that where the evidence was complete

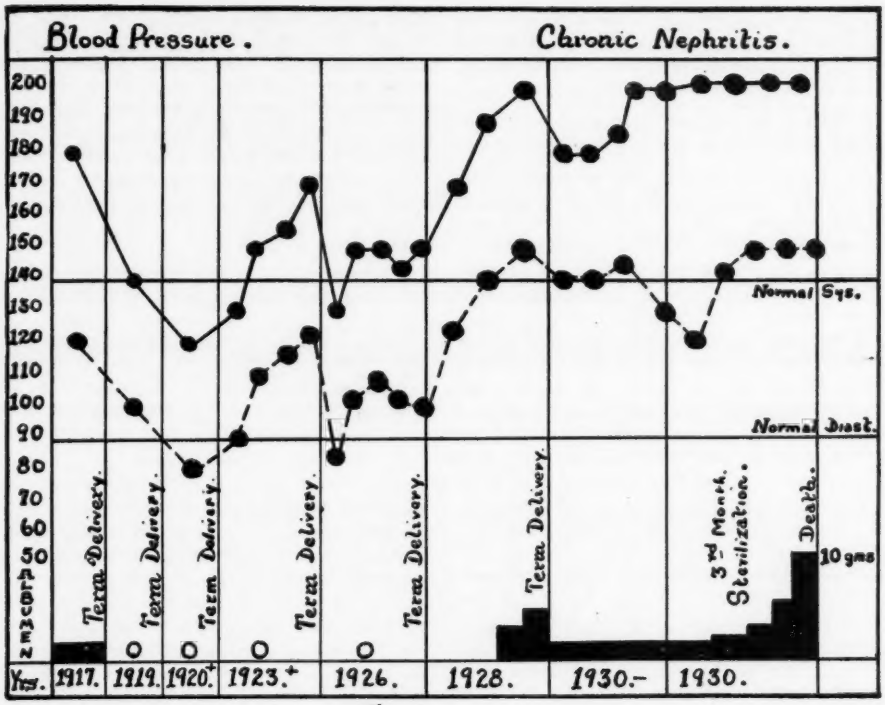

Fig. 1.

and absolute as to the presence of a chronic nephritis seen during a pregnancy we have observed no cure. It should be pointed out that in a certain number of patients the establishment of an absolute diagnosis of nephritis is most difficult, necessitating repeated admissions to the hospital for repeated observations, study, and kidney function tests.

There is a group of pregnant patients who show a hypertension, never very marked, and a slight albuminuria during the last few months of pregnancy, in whom no absolute evidence of nephritis can be elicited and who do not fall into the eclamptic-pre-eclamptic group. For lack of a better term we have called this the "low reserve kidney" group. Stander and Peckham[7] introduced this term in 1926, and so far we have found no evidence to suggest that this group belongs either to the nephritic or the pre-eclamptic class. We are still of the opinion that there are three distinct groups, the nephritic, the pre-eclamptic-eclamptic, and the so-called low reserve kidney group. It is conceivable that the term "low reserve kidney" is inaccurate, but our experience so far is that there is no element of permanent kidney damage (chronic nephritis) or of eclampsia in this group of patients. At the risk of repetition we quote our original description of this group.

LOW RESERVE KIDNEY

"During the last few months of pregnancy, there may appear a moderate rise of blood pressure, usually about 150/90, and relatively small amount of albumin in the urine, ranging from a fraction of a gram to a gram, to very slightly over one gram just before delivery. There may also be some edema and very rarely a complaint of headache. By the end of the puerperium the blood pressure has resumed its normal level, the urine contains no albumin, or only a faint trace, and any edema that may have been present has disappeared. At no time are there any signs of a disturbed blood chemistry, and the nitrogen partition of the urine is normal. In subsequent pregnancies a similar picture may recur. In other cases it may be less severe, but is certainly not worse, while occasionally the patient is entirely normal.

"Pregnancy does not injure this type of kidney, and when we are sure that the toxemia is due to it, we need feel no alarm concerning the course of subsequent pregnancies.

"The outstanding characteristic is the fact that in subsequent pregnancies the patient's condition does not become aggravated and she is as well as, or better than, in the preceding pregnancy. Each of our fourteen cases clearly demonstrates this point."

These characteristics are amply shown in *Fig. 2.*

In the pre-eclampsia, the diagnosis is usually not difficult. The patient's antenatal care is uneventful during the first seven or eight months of her pregnancy. Then we notice a rather sudden and sharp rise in blood pressure, usually accompanied by an albuminuria which may amount to from 2 to 10 or more grams of albumin per liter of urine. In the majority of cases marked edema accompanies the hypertension and albuminuria. The patient may even develop the prodromal symptoms of eclampsia, epigastric pain, partial amaurosis and headache. On admission to the hospital one can elicit no history or evidence of nephritis. The kidney function tests are normal. The blood chemistry is normal except that in the majority of cases there is an increase in uric acid, often amounting to 6 or 7 mg. per 100 c. c. of blood, the normal value being 1.5 to 3.5 mg. If the pre-eclampsia does not develop into actual eclampsia, it clears up completely under treatment or soon after delivery. It, just as eclampsia, does not usually result in damaged kidneys, but about one-fifth of the patients suffering from actual eclampsia with convulsions do sustain injury to the kidneys which is demonstrable months or a year after the attack of eclampsia. By far the majority of eclamptic and all pre-eclamptic patients sustain no kidney damage as a result of the pre-eclamptic-eclamptic disease. As pre-eclampsia is simply an early stage of eclampsia, or virtually eclampsia without convulsions, it should be regarded as the same disease entity as eclampsia, and so should offer no great difficulty in diagnosis. It represents a fairly small percentage of the total number of toxemia patients seen in hospital or private practice. The pre-eclamptic changes are shown in *Fig. 3.*

The diagnosis of a chronic nephritis in a pregnant woman is often exceedingly difficult and at times is almost impossible with our present tests for kidney function. Nephritic patients

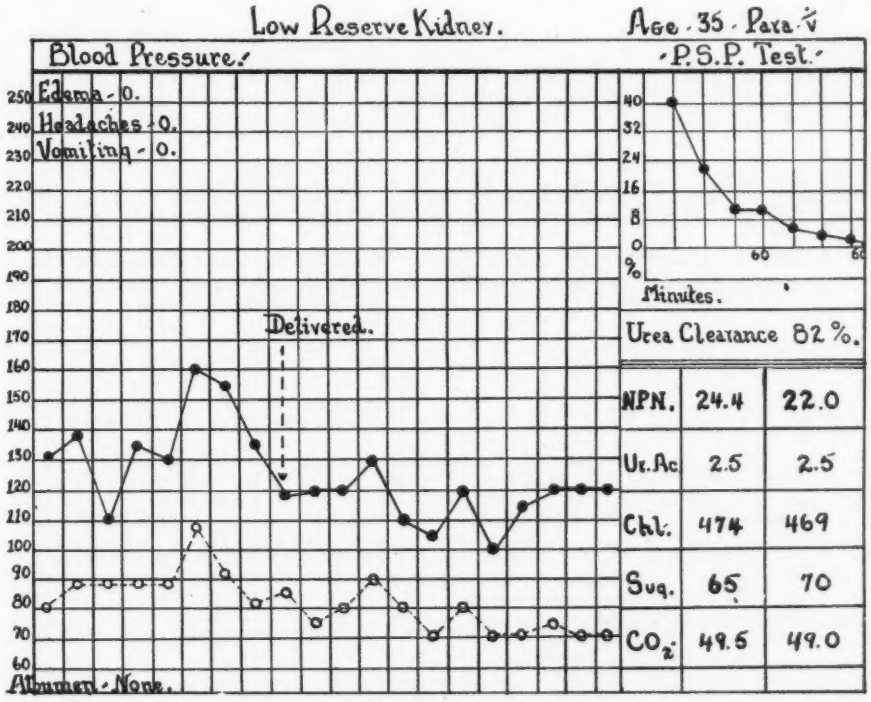

Fig. 2.

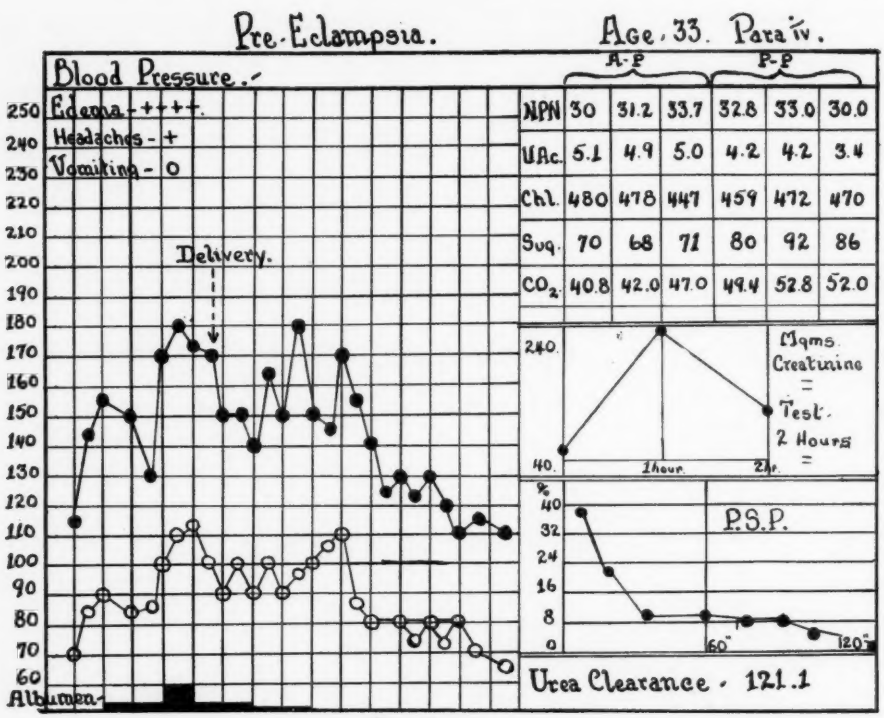

Fig. 3.

may be divided into two groups, one in which the signs, symptoms and laboratory findings admit of a very easy diagnosis because of the severity or stage of the disease, and the other of a very mild or early type where repeated studies are essential to a correct diagnosis. These two groups of patients may perhaps be best exemplified by describing the history and findings in two patients belonging to each of the two groups, respectively.

Case 1, Severe Nephritis Complicated by Pregnancy (Group 1).—The patient is a white woman, aged 23, para 1, gravida 2. Her blood Wassermann is negative. She was registered in the antenatal clinic on August 7, 1933, her last menstrual period having been on May 25, 1933. On examination she appeared to be about 2 months pregnant. Her blood pressure at this time was 200/130 and she had about 4 grams of albumin per liter of urine.

Her past history revealed an attack of scarlet fever at the age of about five years. She was quite well until during her first pregnancy in 1931, when she had "kidney trouble". Her physician at that time told her that she had kidney disease, but that the pregnancy might cure the nephritis. Throughout that pregnancy she suffered from severe frontal headache, constant vomiting, and marked swelling of the face, hands, legs and feet. The pregnancy terminated in a forceps delivery. The child was normal and weighed 3,800 grams. Following this delivery the patient had persistent headache and edema up to the time of her registration in our Out-patient Clinic, about three years later.

Because of the marked hypertension, edema and albuminuria, the patient was admitted to the hospital two days after she registered in the antenatal clinic on August 9, 1933. The findings in the hospital were so striking that a diagnosis of severe nephritis was made and a therapeutic abortion advised. Her blood pressure ranged from 200/130 to 165/110 with an albuminuria of ½ to 2 grams per liter. The urea clearance test gave values of 15.4 and 11.3 per cent on two occasions; the phenolsulphonephthalein test showed almost no excretion of dye and the creatinine test gave further evidence of severely damaged kidneys. The nonprotein nitrogen in the blood ranged between 83.2 and 89.6 mg. per 100 c. c. of blood, and the urea nitrogen between 42.1 and 48.1 mg. The hypertension, albuminuria, edema and headaches, markedly decreased kidney function tests on all occasions and marked nitrogenous retention in the blood fitted in with the diagnosis of severe chronic nephritis.

The only hope to prolong the patient's life slightly lay in a radical procedure. The uterus was emptied by means of a therapeutic abortion on August 12, 1933, three days after her admission. The patient remained

in the hospital for two weeks following the abortion without undue change in the above findings. She was discharged on August 25, 1933, with a blood pressure of 166/110, an albuminuria of 1 gram per liter, edema of the ankles and a nitrogenous retention amounting to 89 mg. of nonprotein nitrogen per 100 c. c. of blood.

She was readmitted to the hospital one month later, on September 25, 1933, with all symptoms and findings more severe. The nonprotein nitrogen gradually rose to 120 mg., the urea-nitrogen to 67.2 mg., and the blood pressure remained at a level of 210/132 with an albuminuria of 4 grams per liter. Her headaches are more severe and the edema is now generalized. Her course now is steadily downhill and soon she will die in uremic coma. This patient's course is graphically shown in *Fig. 4.*

It will be seen that no laboratory tests were actually necessary to establish a diagnosis of chronic nephritis. The past history, the clinical findings, the hypertension, albuminuria and edema, and the patient's failure of response to rest and diet, made the diagnosis quite apparent. The laboratory findings, as above described, corroborated the diagnosis and established beyond a doubt the extreme severity of the disease. This type of patient should admit of no difficulty in diagnosis. It is, of course, evident that this patient should not have been allowed to continue to term with her pregnancy in 1930.

A second patient in this group, although the findings in her case were not so pronounced, is graphically portrayed in *Fig. 5.*

Case 2, Mild Nephritis Complicated by Pregnancy (Group 2).—The patient is a colored woman, aged 20, Wassermann negative, para 0, gravida 1, admitted to the antenatal clinic November 17, 1932, with a blood pressure of 160/90 and no albuminuria. Her last menstrual period was in June, 1932, although she could not give the date with certainty. She had no edema and complained of no symptoms. Because of the hypertension she was immediately admitted to the hospital, where she stayed for a period of 32 days in order that a thorough kidney function study might be carried out. On admission her blood pressure was 160/100 and her urine showed a faint trace of albumin. She appeared to be about 4 months pregnant. Blood chemical studies, repeated on four occasions, were entirely normal, during this admission. The urea clearance test was normal, being 124.3 per cent. A phenolsulphonephthalein test was normal on one occasion and decreased to a level below normal on another. Her blood pressure ranged between 170/100 and 140/78, with an irregular albuminuria ranging from zero to 1 gram per liter. She was discharged on December 19, 1932, with a blood pressure of 136/80 and no albuminuria. The treatment during her stay in the hospital consisted of a low protein, low salt diet with a fluid intake of 2,000 to 3,000 c. c. per day.

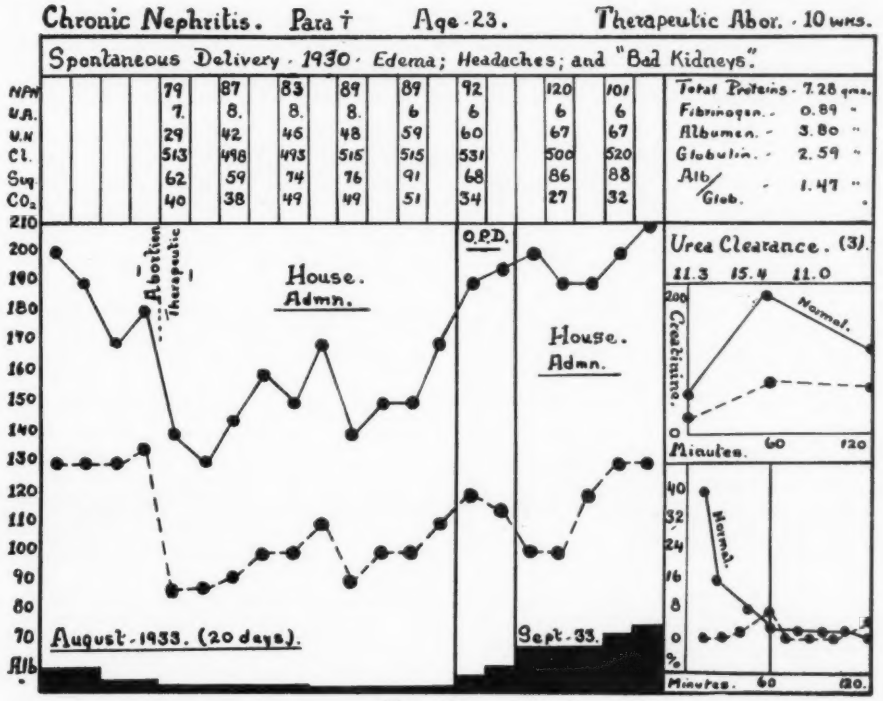
Chronic Nephritis. Para † Age 23. Therapeutic Abor. 10 wks.
Spontaneous Delivery 1930 Edema; Headaches; and "Bad Kidneys".
NPN 79 87 83 89 89 92 120 101
U.A. 7. 8. 8. 8. 6 6 6 6
U.N 29 42 46 48 59 60 67 67
Cl. 513 498 493 515 515 531 500 520
Sug 62 59 74 76 91 68 86 88
CO2 40 38 49 49 51 34 27 32
Total Proteins 7.28 gms.
Fibrinogen 0.89 "
Albumen 3.80 "
Globulin 2.59 "
Alb/Glob. 1.47 "
Abortion Therapeutic
House. Admn.
O.P.D.
House. Admn.
August 1933. (20 days).
Sept. 33.
Urea Clearance. (3).
11.3 15.4 11.0
Creatinine.
Normal.
Minutes. 60 120
Normal.
Minutes. 60 120.

Fig. 4.

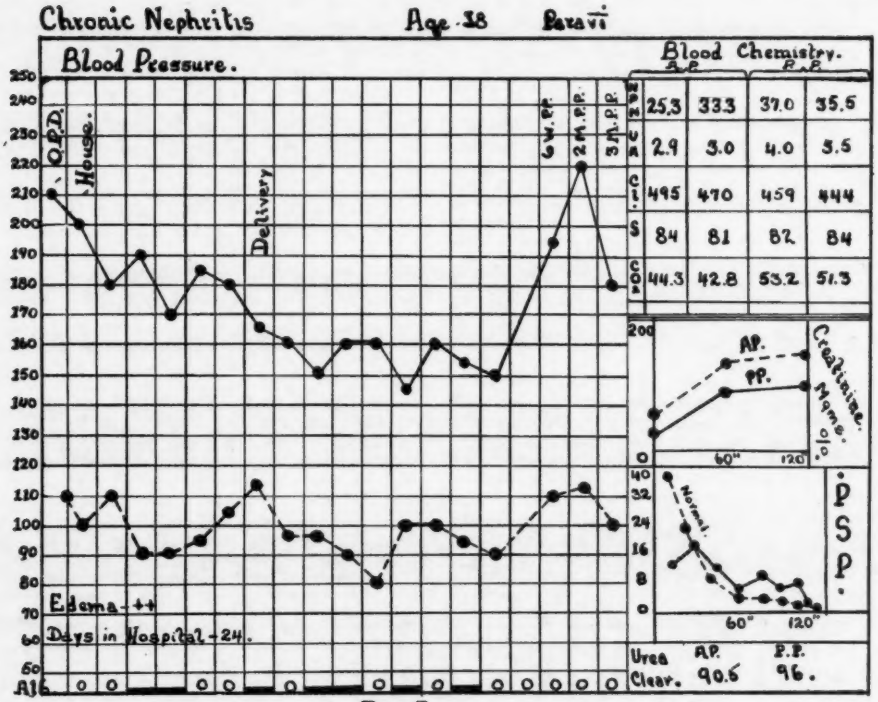

Fig. 5.

She was allowed to go home and was closely followed in the toxemia clinic. In this clinic it was noticed that her blood pressure again rose to 140/90. She was readmitted to the hospital pavilion on January 4, 1933, sixteen days after her discharge. During this admission her blood pressure gradually fell, reaching 120/65 on January 19, the day of her second discharge from the hospital. Her blood chemistry still remained normal, but the urea clearance test, on one occasion, showed a value of 56.9, a definitely low figure. The two other kidney function tests, the phenolsulphonephthalein and the creatinine, each gave abnormally low values at this time. The albuminuria was slight and on discharge had completely disappeared. Never did the patient develop symptoms suggestive of nephritis. On both this second discharge, as well as the first, she was indexed as having an unclassified toxemia. The evidence pointed to a nephritis, but was not definite. At this time we were not justified in making a diagnosis of nephritis.

The patient was again followed in the antenatal clinic, but due to a constantly returning hypertension she had two more admissions to the hospital during this pregnancy. We shall pass over the third admission, as it revealed approximately the same findings as during the second admission.

She was finally admitted on April 12, 1933, being about at term. Her blood pressure was now 140/90. Occasionally she showed a trace of albumin in the urine. There was slight edema of the ankles. During her stay in the hospital at this time the urea clearance ranged between 53.1 and 115 per cent. The phenolsulphonephthalein test was definitely below normal on two occasions, as was also the creatinine excretion test. Blood chemical findings remained normal.

She was delivered spontaneously on May 14, 1933, of a normal male child weighing 2,710 grams. The placenta showed some white infarcts. She remained in the hospital for 22 days after delivery, and was discharged on June 5, 1933, with a blood pressure of 135/102 and a faint trace of albumin in the urine. At this time we made the diagnosis of definite nephritis. The follow-up studies in the postpartum clinic have substantiated this diagnosis. On June 23, 1933, at six weeks postpartum, her blood pressure was 145/90 and her urine showed a trace of albumin. One month later the blood pressure was still at this level and the albuminuria had not cleared up. There was slight edema.

At no time in our repeated studies of this patient were we able to demonstrate the presence of retinitis. The evidence on which the final diagnosis of nephritis was made consists of repeated low values for the kidney function tests, revealed on four admissions to the hospital, all during one pregnancy, a persistent hypertension and albuminuria, present three months after de-

livery, and a complete failure of response to rest in bed and proper dietary measures. The future treatment of this patient should consist of prevention of subsequent pregnancies, either by birth control or sterilization.

We have selected a particularly difficult patient, from a diagnostic viewpoint, to illustrate the manner in which we proceed to establish a definite diagnosis in patients falling into this *Group 2*, or mild nephritic class. It is, of course, not always necessary to have many repeated admissions to the hospital, or a large number of kidney function tests to establish the diagnosis.

TREATMENT

It will be seen that any treatment in *Group 1* is almost hopeless. The renal pathology is too far advanced to admit of much therapeutic help to the patient. The most one may hope to accomplish is slightly to prolong the individual's life by preventing the deleterious effect of pregnancy on the diseased kidneys. The prognosis in this group is grave, the average duration of life of patients belonging in this group, being a matter of one to five years after the diagnosis is made during a pregnancy. As shown in the patient described above (*Case 1*) the interruption of her last pregnancy perhaps slightly prolonged her life, but the kidney disease had progressed too far to allow of any material improvement or arrest by these means.

It is in what we have termed *Group 2*, or the mild, early cases of chronic nephritis complicated by pregnancy, that we believe proper treatment, instituted immediately, may be of great benefit to the patient. These women have not such severe nephritis as to produce nitrogenous retention in the blood, as is often the rule in the *Group 1* patients. With rest in bed, proper diet and termination of pregnancy these patients seem actually to improve, as is demonstrated in the above patient (*Case 2*). We even observe an improvement in the kidney function tests a few months following delivery. This, however, does not mean that the nephritis is cured, but rather that, with the strain of pregnancy removed, the kidneys are able to function at a higher level of efficiency and that the patient's life may be materially prolonged. It is our firm conviction that in patients falling into *Group 2*, in whom we have demonstrated beyond doubt the existence of an underlying chronic nephritis, the best treatment, so far as the life of the mother is concerned, is one including interruption of pregnancy with prevention of future pregnancies.

CONCLUSIONS

(1) The cases of nephritis complicated by pregnancy may be divided into two classes: *Group 1*, comprising severe nephritis; and *Group 2* of mild or early chronic nephritis.

(2) The diagnosis in *Group 1* is relatively simple, based usually on a marked hypertension, albuminuria, nitrogenous retention in the blood, retinitis, headaches, decreased kidney function tests and slight, if any, response or improvement to dietary treatment and termination of pregnancy. In these patients there is usually a history of such an infectious disease as scarlet fever, or of an earlier attack of nephritis or "kidney illness."

(3) The diagnosis in *Group 2* is relatively difficult and can often not be made until after repeated admissions to a hospital for careful kidney function tests. In these patients there is usually no nitrogenous retention and only seldom evidence of retinitis, either spastic or organic. The behavior of the blood pressure and albuminuria over a long period of time gives valuable assistance in the diagnosis. Repeated kidney function tests, especially the urea clearance and the 15-minute phenolsulphonephthalein tests, are of the greatest value in these cases. A low kidney function test, corroborated on three or more occasions, is evidence of damaged kidneys.

(4) A patient suffering from a definitely proven nephritis complicated by pregnancy is not "cured" of the nephritis either during, or after, or by the pregnancy.

(5) We advocate termination of pregnancy and the prevention of future pregnancies as the best and only treatment in patients suffering from a definite and proven chronic nephritis.

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FUNCTIONAL UTERINE BLEEDING*

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There is no chapter in gynecology of more intense interest than that dealing with the evolution of the modern conception of functional uterine bleeding. For many years its etiology was obscure and the theories advanced to explain it had to do chiefly with alterations in the uterus. With our increased knowledge concerning the physiology of menstruation as well as the effects of perversion of this function, the theories based upon uterine changes have been thrown into the discard and at present the universally accepted view is that endocrine disturbances are the chief factors in the production of these menstrual irregularities.

We shall omit a theoretic discussion and limit our remarks to the clinical data obtained from a study of 500 cases admitted to the Gynecologic Service of the University Hospital. In all of them, no pelvic lesion was demonstrable and there was no evidence of a causative constitutional disease. Without exception, the diagnosis of functional bleeding was made only after examination under anesthesia and a microscopic examination of curettings.

Table 1

AGE INCIDENCE

Less than 20 years	4 per cent
20 to 30 years	21 per cent
30 to 40 years	25 per cent
40 to 50 years	41 per cent
50 to 60 years	9 per cent

Nearly one-half of our patients were in the fifth and sixth decades of life. Although it is generally recognized that the incidence of functional bleeding is highest at the two extremes of the menstrual era, only 4 per cent were under twenty years of age. But this series includes only patients with bleeding of sufficient severity to require hospitalization and the small number seems to emphasize the fact that a large proportion of adolescent hemorrhages cease spontaneously or respond to appropriate treatment and that surgical procedures are seldom required.

*Read in Section on Gynecology, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

Of the 44 patients between fifty and sixty years of age, uterine bleeding recurred in 10 after one or more years of postmenopausal amenorrhea. Whether these should be included as types of functional bleeding is open to question, but the absence of pelvic disease, the character of the endometrium and the subsequent clinical course seemed to justify the diagnosis. Of particular interest is the fact that the endometrium in five of these postmenopausal patients showed typical hyperplasia. If the prevailing conception is correct that endometrial hyperplasia is due to persistent follicular stimulation, its occurrence in the postclimacteric years is difficult to explain since the ovaries are atrophied and functionless. Taylor suggests that these hyperplastic changes are "but remnants of a typical hyperplasia persistent since the menopause," but it seems unlikely that this structure alone should escape the atrophy found in other pelvic organs. That it may be of hormonal origin is suggested by Frank's statement that "in a number of women long past the menopause the hormone content of the blood was exactly as we find it in young menstruating women." The experimental work of Hartmann and his associates is particularly suggestive since they have shown that in castrated animals hyperplasia and uterine bleeding can be produced by the administration of anterior pituitary hormones. Fluhmann's demonstration of increased pituitary activity after the menopause adds another link to the chain of evidence favoring the hormonal origin in certain cases of postclimacteric bleeding.

UTERINE BLEEDING

Menstrual irregularities at the time of or in the space of a few years after puberty are often prophetic of similar irregularities later in life.

Table 2

RELATIONSHIP BETWEEN THE EARLY MENSTRUAL HISTORY AND THE DEVELOPMENT OF FUNCTIONAL UTERINE HEMORRHAGE

Number patients with definite early menstrual history	461
Patients with abnormal early menstrual history	37 per cent

These abnormalities include prolonged intervals of amenorrhea followed by flooding or sustained bleeding, menorrhagia with normal or shortened intervals and intermenstrual or totally irregular bleeding. We do not know the incidence of such early irregularities in women whose later menstrual history is normal, but we believe it is much less than the 37 per cent

here recorded. It suggests that in many of these patients with functional bleeding there is an inherent endocrine imbalance which for a time is restored to normal, but later reasserts itself and finds expression in abnormal menstruation, sterility or repeated abortions.

Table 3

THE TYPES OF BLEEDING ENCOUNTERED

(A) Menorrhagia, normal interval	13 per cent
(B) Menorrhagia, short interval	25 per cent
(C) Totally irregular bleeding	19 per cent
(D) Regular periods, followed by continuous bleeding	8 per cent
(E) Irregular periods, followed by continuous bleeding	11 per cent
(F) Progressive menorrhagia to metrorrhagia	10 per cent
(G) Amenorrhea followed by continuous bleeding	11 per cent
(H) Mid interval bleeding with normal periods	3 per cent
Total cases with menorrhagia, A to B (inclusive)	38 per cent
Total cases with metrorrhagia, C to H (inclusive)	62 per cent

An analysis of the types of bleeding shows that the various forms of metrorrhagia are almost twice as common as menorrhagia, although the prolonged, profuse period with shortened intervals is the predominating individual type. It is evident from this analysis that functional bleeding is not characterized by any one type and that frequently it differs in no respect from that associated with pathologic states, especially the abnormalities of early pregnancy, pelvic infection, myoma, and carcinoma of the uterus or adnexa.

With but little or no demonstrable pathology, one is at a loss to explain satisfactorily the profuse and at times alarming hemorrhage which functional disturbances may produce. Schroeder, Fluhmann and others ascribe the bleeding in endometrial hyperplasia to areas of necrosis or injury to large superficial vessels. But the explanation does not seem adequate since with normal menstruation the entire superficial layer of endometrium is cast off. Novak states that increased permeability of the uterine blood vessels must be considered as a possible cause, but he seems more inclined to ascribe it to some extra-pelvic influence, what he terms "the bleeding factor" with which the hypophysis may be intimately concerned. The fact that profuse bleeding may occur from normal or even atrophied endometrium as well as from the hyperplastic type, and that hyperplasia is not infrequently found in cases of amenorrhea, warrants the conclusion that the condition of this structure plays but a minor role in the causation of bleeding. Novak's "bleeding factor" theory is based upon a certain amount of experimental evidence, but we believe he comes nearer the truth when he ascribes the bleeding to some defect in the vascular supply of the uterus.

Table 4

STERILITY

THE INCIDENCE OF STERILITY IN FUNCTIONAL BLEEDING AND IN HYPERPLASIA

	Sterility
Recognized incidence at large	10 per cent
Incidence with hyperplasia	29 per cent
Incidence with normal endometrium	20 per cent

One-fifth of the married women in this series were sterile, which doubles the recognized incidence at large. Of the 282 women whose curettings showed no hyperplasia, 20 per cent were sterile. Because of the ovarian defects which are associated characteristically with endometrial hyperplasia, we had anticipated a much higher sterility incidence than in the preceding group, but such was not the case, since it rose to only 29 per cent.

Table 5

THE ENDOMETRIUM

RELATIONSHIP OF THE TYPES OF BLEEDING TO THE ENDOMETRIAL CURETTINGS

	Number Patients	Normal Endometrium Per Cent	Hyperplasia Per Cent	Insufficient Tissue Per Cent	Edema Endometrii Per Cent	Chronic Endometritis Per Cent
Menorrhagia	190	76	12	10	1.5	0.5
Metrorrhagia	310	56	30	10	1.5	2.5

Incidence of hyperplasia in entire series, 23 per cent.

Hyperplasia of the endometrium was found in less than one-fourth of our patients. What proportion of sections diagnosed normal endometrium of the interval pattern belonged to the non-cyclic type is impossible to say; efforts to determine this met obstacles which were insuperable. Chronic endometritis showed an incidence of but 1 per cent; in none of these patients was there any clinical evidence of pelvic infection and a recent intrauterine instrumentation was the usual history. Despite thorough curettage, a number of specimens contained insufficient tissue for microscopic diagnosis and doubtless at least a portion of these were instances of atrophy of the endometrium. This finding was distributed through all the age groups and not confined to the postmenopausal

era. Our analysis shows that in both menorrhagia and metrorrhagia, the endometrium was normal in the majority of cases. Hyperplasia was found in but 12 per cent of the menorrhagia group and 30 per cent of the metrorrhagias. Divided according to age, we find that hyperplasia occurs most frequently at the two extremes of the menstrual life: 40 per cent in patients under twenty years of age and 36 per cent in those between fifty and sixty.

The inconstancy of the endometrial picture and the low incidence of hyperplasia are the striking features of this study. The endometrium affords an accurate index of pituitary and ovarian function, since under normal conditions the varying phases it exhibits during the cyclic transformation are the expression of coordinated hormonal stimulation from these glands. With perversion of this stimulation, both in degree as well as kind, the endometrial response must likewise vary, and upon this depends the diversity of its histologic architecture. This variation in the endometrial picture is strong proof that all cases of functional bleeding cannot be ascribed to identical hormonal defects.

Diagnosis.—The functional origin of irregular uterine bleeding is to be suspected when it occurs during the menstruating age and when the routine general and pelvic examinations reveal nothing to explain it. However, the final decision must often be held in reserve until warranted by the proof afforded by further investigation. Menorrhagia with no suggestion of bleeding during the intervals is the most common individual type of functional bleeding; it is never of malignant origin, and under such circumstances one may rest assured of its functional nature and institute appropriate medical or hormonal therapy. The situation is entirely different in the presence of metrorrhagia which is always a danger signal, particularly in the latter half of the menstrual life. Here malignancy or some other organic lesion is the more likely cause of the bleeding and no form of treatment is permissible until the exact condition of affairs has been determined by examination under anesthesia, with a curettage and microscopic study of the curettings.

Pain is rarely a symptom in uterine bleeding of the functional type; dysmenorrhea is likewise uncommon, but may accompany profuse bleeding with the passage of clots. When pain is present, some organic lesion, such as chronic adnexitis or endometriosis, should be suspected.

The characteristic feature of the pelvic examination in cases of functional bleeding is the absence of gross pathology. Often, however, certain minor changes are detected. The cervix may be somewhat softened, slightly dilated and faintly discolored; increased succulence may also be manifest in the vagina. Moderate, diffuse uterine enlargement is not uncommon and in a considerable proportion of the cases one or both ovaries will be found larger and perhaps more tender than normal, due to the presence of single or multiple follicular cysts.

A small submucous myoma, deeply placed and concealed by the overlying uterine musculature, may give rise to identical symptoms and may easily escape detection. However, its presence is usually indicated by irregularity in the contour and consistency of the uterus or the curette may reveal its protrusion into the endometrial cavity. Irregular bleeding is commonly associated with a chronic adnexitis, and is due in large part to defects in ovulation incident to a peri-oophoritis. A history of previous acute pelvic infection, the characteristic stigmata of chronic gonorrhea, slightly enlarged, adherent adnexae and pain, usually point the way to a correct diagnosis. Even the minor lesions of endometriosis can give rise to irregular bleeding; one or both ovaries may be enlarged, nodular and adherent, and small nodulations are often palpable in the cul-de-sac. An acquired dysmenorrhea of the menstrual or premenstrual type is a characteristic symptom. In each of the lesions just mentioned, altered ovarian function is a potent factor in the production of irregular menstruation, but this functional disturbance is secondary to or associated with an organic lesion which often requires treatment of an entirely different nature from that appropriate to true functional bleeding. Hence the importance of their differentiation.

As already stated, softening, dilatation, and even slight discoloration of the cervix may exist in these cases and when such findings are associated with a history of amenorrhea followed by prolonged bleeding, differentiation from an early miscarriage is difficult or even impossible without a curettage. A polycystic ovary or a single follicular cyst is not uncommon in functional bleeding; rarely, such ovaries are exquisitely tender and may produce sharp attacks of pain. Under these circumstances, a history of amenorrhea and continuous bleeding presents a clinical picture which closely simulates that of tubal pregnancy. For obvious reasons, carcinoma of the cervix is not confused with functional bleeding unless of the intracervical type. Carcinoma of the fundus is essentially a postmenopausal disease, but an analysis of the cases from our

clinic made by Norris and Vogt shows that 17 per cent were of premenopausal age. Its differentiation from functional bleeding is made possible only by a diagnostic curettage and examination of the curettings.

In rare instances, functional bleeding occurs as a postmenopausal manifestation, but this diagnosis should be made with reservation and only after the possibility of uterine or adnexal carcinoma has been eliminated by all available methods of examination. In this connection, granulosa cell carcinoma of the ovary deserves particular mention, since it usually develops after the menopause and is characterized by a return of bleeding and hyperplasia of the endometrium.

Irregular menstruation may be but the local expression of some constitutional condition such as cardiovascular disease, chronic nephritis, hypertension, blood dyscrasia, *et cetera*, and such possibilities must be eliminated before the diagnosis of true functional bleeding is made. Diminished activity of the thyroid gland may produce menorrhagia, but, conversely, our experience has shown that patients with functional bleeding usually present no striking evidence of thyroid abnormality. In the functional hemorrhages of adolescents, Plass emphasizes the fact that even minor degrees of hypothyroidism are significant.

Our experience with hormonal tests has convinced us that they are of little or no value in the diagnosis of functional bleeding. On the other hand, a study of the endometrium at weekly intervals does afford valuable information regarding endocrine activity or defects. The suction cannula devised by Burch has proven a satisfactory means of obtaining the endometrial specimens.

Treatment.—If we could devise an ideal method of treating this type of uterine bleeding, it would have for its results preservation of the menstrual and procreative functions in women under forty, and the return of normal periods or amenorrhea without severe menopausal symptoms in women beyond this age. Unfortunately, the methods at our disposal often fall short of this ideal, but in our choice of treatment we should attempt to approach it as nearly as possible. Only too often methods are employed with the control of bleeding as the only objective, and with entire disregard of the disastrous sequelae which may accompany the induced menopause.

In many of the milder forms of functional bleeding, the blood loss is insufficient to require treatment. Change of climate, occupation or mode of living will occasionally be followed by a resumption of normal menstruation or the menstrual irregularity may cease for no explainable reason. Such is often the case in adolescents; the same may be said to occur during the menopausal age, but here the more likely cause of irregular bleeding is a myoma or cancer and hopeful expectancy is warranted only when these organic lesions have been eliminated as possibilities.

Until very recently the control of profuse or continuous bleeding in young women has been a difficult problem. The value of thyroid extract in adolescents is well recognized, but with this exception, hormonal therapy has been futile. With the introduction of the anterior pituitary luteinizing substance as a therapeutic agent, sufficiently encouraging results have been reported to warrant its adoption. Our experience with it is limited to 39 cases. Twenty-three of these were less than thirty years of age and in two-thirds of this group the bleeding was satisfactorily controlled for three months or more and unaffected in one-third. Six patients were between thirty and forty years of age and the treatment gave no relief in four. Of the ten in the fifth decade of life, none received any benefit. This small number of cases does not permit of any conclusion, but the results obtained confirm the statements of Novak, Mazer and others as to the value of prolan therapy in young women and its futility after forty years of age.

With failure of hormonal or other forms of medical therapy, the methods of treatment at our disposal consist of curettage, irradiation and hysterectomy, all far from ideal procedures. The proper decision as to which method should be employed cannot be made without a full appreciation of the advantages and limitations inherent to each. The criteria of success or failure vary in accordance with the age of the patient. In young women, success is measured in terms of normal menstruation and preservation of the reproductive function, while in women of menopausal age, the treatment may be considered successful when complete cessation of these functional activities occurs. Since one-half of the patients are under forty years of age, the importance of these considerations is manifest.

The modern conception of the causes underlying functional bleeding casts discredit upon curettage as a therapeutic measure and explains its frequent failures, but the fact remains that curettage may be efficacious and it has a place in the treatment of this type of bleeding. This

applies in particular to the treatment of young women in whom one may hesitate to use radium. At least a few will be temporarily benefited or cured. With temporary relief, the curettage may be repeated in the hope that sooner or later normal menstruation will become established. Because of the uncertain results attending curettage, the patient should be fully informed of what she can expect.

After forty years of age and when other methods have proven unsuccessful in younger women, radium or roentgen therapy is indicated. We prefer radium because its dosage can be more accurately regulated and the beneficial effects are in part due to its local action upon the uterine blood vessels. Further, with radium, completion of the treatment is accomplished at the time of the diagnostic curettage which should precede either form of irradiation in most instances.

Radium therapy deservedly occupies a prominent place in the treatment of functional bleeding and in women of menopausal age it approaches the ideal. It has also proven of value in younger women, but here one must appreciate its limitations and dangers if disastrous sequelae are to be avoided. Since the cure of bleeding by radium is accomplished largely through its effect upon ovarian function, an evaluation of radium therapy must take into consideration not only the control of bleeding, but also the manifestations which have arisen incident to disturbance of this function. With this standard as a guide, we have recently analyzed our results of radium treatment and we present the conclusions which this study seems to warrant.

CONTRAINDICATIONS TO RADIUM

Profoundly anemic patients react poorly to both radium and roentgen therapy and either form of irradiation should be withheld until the blood has been improved by transfusion and other appropriate treatment. Indeed, blood transfusion may prove curative, as we have had occasion to observe in a few cases of adolescent hemorrhage.

Pemberton has called attention to the danger of radium in patients who have had a previous pelvic operation, since an intestinal loop adherent to the uterus may be seriously damaged by the rays. In a few such instances, we have given short applications of heavily filtered radium successfully, but we prefer operation or roentgen therapy.

The absence of intermenstrual pelvic pain and severe acquired dysmenorrhea is characteristic of functional bleeding. When pain is an associated symptom, some organic lesion is usually present, even though examination fails to reveal it and operation is preferable to radium therapy. With surprising frequency the wisdom of this decision will be proven when the abdomen is opened.

The highly nervous woman is ill adapted to both radium and roentgen therapy because of the distressing sequelae which frequently attend the induced menopause. In this type of woman hysterectomy with ovarian conservation yields better results.

When radium is indicated, the initial dosage is of paramount importance. This decision depends not only upon the incidence of controlled bleeding which can be anticipated from a given dosage, but also upon the incidence of amenorrhea and severe menopausal symptoms which will accompany this dosage. Our analysis emphasizes certain general principles which are pertinent. Individual variation in susceptibility to the effects of radium are not uncommon and, for obvious reasons, this fact is of importance in treating young women. When analyzed in groups and by decades, our findings suggest that between twenty and thirty the ovaries are resistant or they possess a strong recuperative power, for in not a single instance did a permanent amenorrhea develop despite the fact that some of these patients had been given a fairly large dosage. Increased susceptibility to radium begins after thirty and gradually increases, reaching its height in patients who continue to menstruate after fifty. Further, the incidence of permanent amenorrhea and severe menopausal symptoms runs parallel until forty, when, as amenorrhea increases with a given dosage of radium, severe menopausal symptoms decrease until between fifty and sixty, the incidence of these symptoms is almost negligible.

From our study of the effects produced by varying initial dosages during the different decades, we have drawn conclusions which govern us in our work and these will be briefly summarized:

Radium is rarely indicated in the treatment of patients under twenty years of age. When it is found necessary, the initial dosage should not exceed 200 milligram hours.

Between twenty and thirty, our results show that a dosage of 400 milligram hours can be administered safely. This dosage will be more than 80 per cent efficient in the control of bleeding, but a few patients will develop a temporary amenorrhea of a few months' duration. Should the bleeding persist, the dosage can be increased by 100 milligram hours.

Our analysis of the group between thirty and forty brings out the important fact that with increasing dosage there is a rapidly increasing incidence of menopausal manifestations. With a dosage of between 800 and 1,200 milligram hours, permanent amenorrhea occurred in 56 per cent and severe menopausal symptoms in 47 per cent of the patients. An initial dosage of 300 milligram hours will control the bleeding in 80 per cent and without permanent amenorrhea. Should re-radiation be necessary, an application of not more than 400 milligram hours should be administered, and if this fails, we favor hysterectomy with conservation of ovarian function rather than increased irradiation.

Functional bleeding occurs most frequently between forty and fifty years of age, and because these women are approaching the time when, in the normal course of events, functional activity will cease, the administration of a menopausal dose of radium has come into common usage. We believe this is a mistake because of the high incidence of severe menopausal symptoms. In women near forty, we are using a 400 milligram hour dosage. Should this and a re-radiation dosage of 500 milligram hours fail, a hysterectomy is advised. In women near fifty, increased radium dosage can be used because the incidence of severe menopausal symptoms attending it will more nearly approximate that of the uninduced menopause.

Between fifty and sixty years of age, the results of radium therapy approach perfection. Maximum dosage can be given, since severe menopausal reactions rarely develop.

In conclusion, we would again emphasize the statement that the value of radium therapy must be measured not only in terms of bleeding control, but also of the menopausal symptoms which are produced by it. When other methods have failed to control functional bleeding, radium therapy is the best method at our command, but it has its limitations and should not be used to the exclusion of operation when these limitations have been reached.

We are indebted to Dr. C. C. Norris for his valuable assistance in the study of the endometrium.

THE TREATMENT OF EDEMA IN CONGESTIVE HEART FAILURE*

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The onset of congestive heart failure is admittedly an omen of serious significance regardless of the type of heart disease which it complicates. A knowledge of the etiology of the primary heart disease is of great importance in estimating the prognosis. It is well known that the duration of life after congestive failure has intervened is relatively long in rheumatic heart disease and very short in syphilitic heart disease, while the outlook in the degenerative types, hypertensive and arteriosclerotic, occupies an intermediate position. Such other factors as occupation (sedentary or strenuous, before and after the development of decompensation), age, sex, social conditions, the cooperation of the patient, are also of importance in determining the future progress of the condition and its outcome. Despite the rather gloomy prognosis for the cardiac patient after the beginning of congestive heart failure much may be accomplished both subjectively and objectively by adequate treatment. In some instances the results of therapy are very striking, especially in those cases with marked edema.

It is our purpose at present to discuss particularly the treatment of the edema of congestive heart failure, and especially the massive edema of cardiac origin. This type is due largely to an increase in filtration through the capillaries which results from the increased venous pressure accompanying congestive failure. Increased permeability of the capillary walls due to anoxemia also facilitates the passage of fluid into the tissue interstices. In some instances other causes stand in the role of contributory factors, more especially nutritional influences and impaired renal function.

Herrmann[1] has investigated the nutritional influences in a large number of congestive failure patients with the various types of heart disease,

*Read in Section on Medicine, Southern Medical Association, Twenty-Sixth Annual Meeting, Birmingham, Alabama, November 15-18, 1932.

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and has found that a high percentage showed considerable lowering of the total blood proteins, but seldom was the figure obtained below the edema level. In the same study, even after profuse diuresis and the subsidence of other congestive failure phenomena, the blood proteins still remained at approximately the same level, or had risen but slightly, except where definite nutritional disturbances had also been present (alcoholism, starvation). It is believed, therefore, that nutritional factors exert only a slight and secondary effect in the development of cardiac edema in most instances.

Impaired renal function is, at times, an important obstacle in the management of congestive failure patients. This is particularly true of those cases in which the primary heart disease results from or is accompanied by vascular hypertension with resulting glomerular injury. An associated renal insufficiency may also increase the degree of edema in congestive heart failure. Studies of renal function by the usual methods will readily disclose the cases in which this factor is present. When patients are first seen in congestive heart failure it may be impossible to determine whether lowering of renal function is due to structural change in the kidneys, or to passive congestion. If due to passive congestion, renal function returns to normal with the relief of congestive failure, whereas such improvement does not occur if the lowering of renal function is due to structural changes.

Edema is, of itself, a distinct impediment to recovery from, as well as a result of, congestive heart failure. The water-logged tissues render the circulation through them more difficult, and thus throw an additional burden upon the already insufficient myocardium. Harrison and Pilcher[2] have presented convincing evidence that edema diminishes the diffusion of oxygen from capillaries to the tissues (diminished tissue oxygen tension) with a secondary and compensatory increase in blood flow, but withal a decreased oxygen utilization. Simultaneously, carbon dioxide increases in the tissues. They conclude that edema while "itself a symptom of congestive heart failure, throws an additional load on the heart, and is thus secondarily a further cause of heart failure." On the basis of these studies it is pointed out that the congestive failure patient at rest suffers as much from general circulatory inefficiency as from myocardial insufficiency. It is thus apparent that in those patients with congestive failure in whom the edema remains in spite of the usual therapeutic methods, relief from the cardiac insufficiency may not be obtained until removal of the edema is accomplished.

Clinical observations in patients with congestive heart failure in whom dyspnea, tachycardia, cyanosis, and venous stasis remain unaltered after bed rest and digitalization, often show that these symptoms disappear with, but not until, the edema is removed. A striking demonstration of the effect of edema upon cardiac function is presented by the relief afforded in cases of resistant paroxysmal nocturnal dyspnea following diuresis. With these facts in mind, the indications for the removal of edema are impressively emphasized, and this can be obtained in many instances only by the intelligent use of diuretic drugs.

Clinical studies of diuretics and investigations of the mechanism of diuresis in certain edematous patients with heart failure, especially those who are refractory to the ordinary measures, have been made.

The importance of bed rest in the treatment of myocardial insufficiency cannot be overemphasized. It cannot be measured quantitatively, but is of itself sufficient to cause a marked diuresis in some cases. Three days of rest in bed in the hospital have been routinely allowed as a control period. During this time a salt-poor, low protein diet has been given, the fluid intake maintained at 1,500 c. c. per 24 hours, and the urine output and daily body weight have been recorded. After this preliminary rest period the next study has been concerned with the effect of digitalization which has usually been accomplished within 24 hours. The urine output, the body weight and changes in the degree of edema have been noted. In most patients with slight to moderate edema this regime is followed by a sharp diuresis which removes practically all of the abnormally accumulated fluid. In those with anasarca the diuresis resulting from digitalization may be unusually prolonged, and in such instances may or may not render the patient edema free. It is in those cases in which edema persists after bed rest and digitalization that the action of various diuretic drugs may best be studied.

XANTHINE DIURETICS

As emphasized by Christian,[3] theophylline (theocin) is the most efficient of the xanthine diuretics for oral administration. It can be given in doses of five grains (0.3 gram) three or four times daily for two or three days, after which it is best discontinued for a few days to prevent the occurrence of nausea and vomiting.

Some patients tolerate the continuous administration of theocin over relatively long periods. An occasional case has responded well to theobromine calcium salicylate (theocalcin), which is less likely to produce gastric irritation but, like theobromine sodio-salicylate (diuretin) produces less striking diuresis than does theocin.

Theophylline ethylene diamine (thephyldine) is only occasionally effective as a diuretic when given by mouth in the usual doses, and is only slightly more so when administered subcutaneously or intramuscularly. Intravenously, however, in doses of 7.5 or 15 grains (0.48 or 0.96 gram) theophylline ethylene diamine is the most efficacious of the xanthines, and at the same time it is one of the safest of the spectacular diuretics. When the maximum dose, 15 grains (0.96 gram) is given, it has been considered advisable to divide the total amount into two equal doses of 7.5 grains (0.48 gram) to be injected at least one hour apart. There is but one disadvantage to the use of theophylline ethylene diamine intravenously, namely: the slight reaction which almost invariably occurs with its injection. This reaction is in all respects similar to that produced when certain calcium salts are given intravenously, and consists of a sense of heat over the body, tingling, a feeling of impending collapse, rapid pulse, dyspnea, and occasionally nausea and vomiting. If the drug is diluted with 10 to 20 c. c. of physiological sodium chloride solution, and is administered slowly, these untoward symptoms may be minimized. Despite the discomfort which accompanies the intravenous injection not a single alarming or serious reaction has been observed among the many patients to whom it has been given.

In a large series of diuretic studies using theophylline ethylene diamine, the time of onset of the diuresis was practically always within the hour, reaching its maximum in 3 or 4 hours, at which time the rate of urine secreted per minute averaged about 7 c. c. The complete diuretic effect is usually dissipated within 12 hours, but occasionally it persists into a second 12-hour period.

In extensive studies of patients with congestive heart failure, using the creatinine method of Rehberg, elsewhere reported in preliminary form, [4 5] a distinct augmentation of glomerular filtration, with slight decrease in tubular resorption as the *modus operandi* of xanthine diuretic action has been demonstrated. These re-

Table 1

R. W., colored male, aged 61. Arteriosclerotic heart disease with congestive failure. March 10, 1932, creatinine 5 gr. at 7:00 a. m. and thephyldine I. V. 0.48 gr. at 9:30 a. m. and 10:30 a. m.

TIME	INT Interval in minutes	VOL Urinary output in c.c. volume	U Rate of flow per minute	NaCl UX Urinary NaCl mg. per 100 c.c.	NaCl BX Serum NaCl mg. per 100 c.c.	CO_2 Vol. percent in serum	Ur UX Urinary urea mg. per 100 c.c.	Ur BX Serum urea mg. per 100 c.c.	Cr UX Creatinine in urine mg. per 100 c.c.	Cr BX Creatinine in serum mg. per 100 c.c.	C Concentration index Cr U % / Cr S %	F Calculated glomerular filtration rate C x p	R Calculated tubular reabsorption rate, F-U	F Cl Diam. filtr. of NaCl F X Cl S % / 100	U Cl Urinary exc. of NaCl U X Cl U % / 100	R Cl Tub. reabsorp. of NaCl FCl - UCl.	C1R % Percent NaCl in R R Cl X 100 / F	EC1 % Percent of FCl exc. UCl X 100 / FCl	CC1 Concentration ratio of NaCl ClU % / ClS %	FU Glom. filtr. of urea F X U S % / 100	UU Urinary exc. of urea U X U U % / 100	RU Reabsorbed urea FU - UU	Ur Percent urea in R RU X 100 / FU	EU Percent of FU exc. UU X 100 / FU	CU Urea conc. ratio UU % / US %
U 6AM-7AM Bl 7 AM	75	78	1.04	330	544	60	500	18.7	87	1.67	52.	54.2	53.2	295	3.44	291.6	547	1.17	0.6	10.15	5.2	4.9	9.2	51.4	26.8
U 8:20 Bl 8:30	65	37	0.57	297	495	54	462	24.	247	2.61	94.8	53.8	53.2	266	16.9	249.	468	6.35	0.6	12.9	2.64	10.3	19.3	20.4	19.2
U 9:20 Bl 9:20	60	200	4.67	462	578	51	154	20.7	144.5	3.75	38.5	180	175.3	1040	21.5	1019.	580	2.06	0.8	37.2	7.2	30.0	17.1	19.3	7.48
U 10:42 Bl 10:30	82	778	9.50	462	528	59	123	30.	107.5	3.34	32.2	306	297.5	1620	43.8	1576	530	2.71	0.87	92.0	11.7	80.3	26.8	12.7	4.1
U 11:45 Bl 11:20	63	445	7.07	363	560	58	218	21.4	108.5	3.75	29	205	198.	1150	25.6	1124.	578	2.22	0.65	44.1	15.4	28.7	14.5	34.9	1.02
U 12:45 PM Bl 12:30	55	280	5.10	462	560	55	172	21.4	77.	2.40	32.1	164	158.9	920	23.5	897	565	2.56	0.83	35.1	8.76	26.3	16.6	25.0	0.8
U 2:15 Bl 2:00	95	330	3.48	528	478	51	120	21.4	84	2.50	33.6	117.	113.5	560	16.4	542	477	3.28	1.1	25.0	4.17	20.8	18.3	16.7	5.6
U 4:10 Bl 4:00	115	303	2.64	1090	396	60	123	20	76.5	2.40	31.9	84.3	81.7	332	28.8	303	375	8.68	2.75	16.9	3.25	13.6	16.6	19.2	6.15
U 6:10 Bl 6:00	120	260	2.16	990	214	57	150	23.1	79.5	2.31	34.4	74.4	72.2	159	21.4	128.	177	13.5	4.63	17.2	3.24	14.0	19.4	18.8	6.5
U 6 PM to 6 AM Bl 8 A.M.	720	910	1.26	990	428	58	133	17.6	72	1.25	57.5	72.8	71.2	312	12.5	300	420	4.0	23	12.75	1.66	11.1	15.6	13.2	7.6

sults are in accord with those previously obtained by Schmitz and Leiter, using the same diuretic in normal dogs (*Fig. 1*). This is believed to be the result of increased blood flow through the dilated glomerular tuft, and corroborative support of this view is found in the experimental studies of Medes, Herrick and Baldes.[6] These investigators applied the direct Rein Thermo-Stromuhr method to the study of the blood flow through the kidney before and during the action of various diuretics. Our similar studies by the same method during the diuresis of digitalization (*Fig. 2*) afforded convincing evidence that increased glomerular filtration with a concomitant slight decrease in reabsorption was likewise operative under such conditions.

MERCURIAL DIURETICS

That mercury has long been recognized to possess diuretic properties is attested by the traditional reputation and the continued popularity of the Guy's pill* in edema refractory to digitalis alone. The search for a relatively safe mercurial that could be used intravenously in the treatment of syphilis resulted in the incidental but most significant and far more important discovery of the tremendous diuretic value of novasurol (merbephen) and salyrgan (mersalyl).

Novasurol.—It is probably no exaggeration to state that novasurol is the most powerful of any diuretic yet introduced; however, its use has been greatly limited due to contraindications and the unexpected occurrence of toxic effects such as stomatitis, colitis and acute hemorrhagic nephritis, even in carefully selected cases. In view of these facts salyrgan has, by general consent, almost entirely displaced novasurol. While salyrgan is generally efficient and relatively safe, it should not be concluded that harmful side effects never occur following its use. It can usu-

*Guy's pill is composed of blue mass, powdered digitalis, squills and extract of hyoscyamus, each 1 grain (0.065 gram).

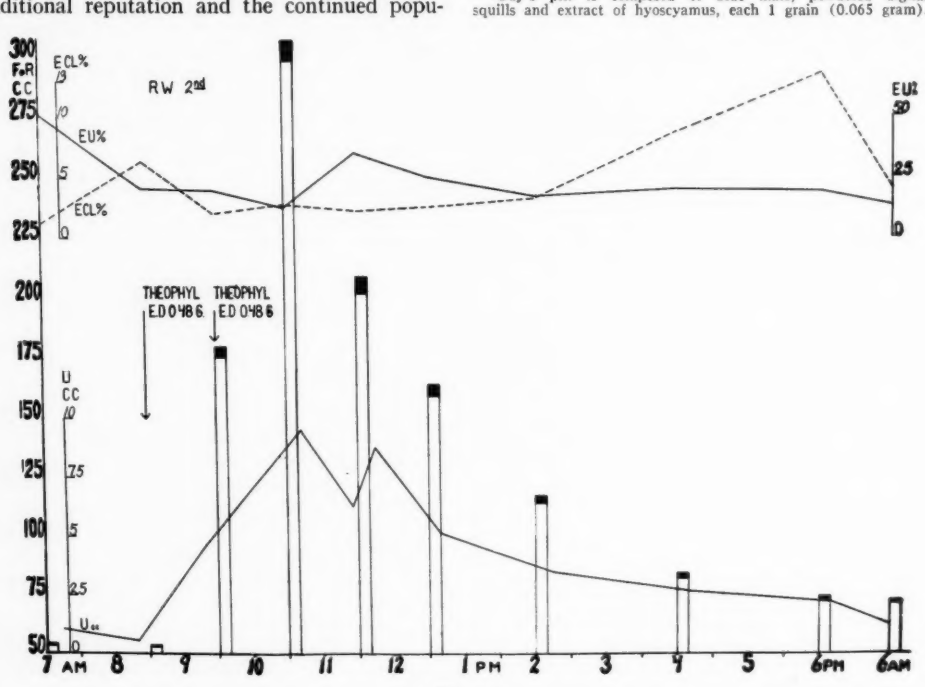

Fig. 1

(R. W., second study). A schematic representation of the filtration (F) and reabsorption (R) during the second theophylline ethylene diamine diuresis (Clinical Chart No. 7, J.A.M.A.) studied by the creatinine method of Rehberg (The data are given in Table 1, Theophylline ethylene diamine diuresis). The top of each column represents the filtration in c. c. per minute; the black cap represents the urinary excretion per minute, and the difference between these two, the remaining unshaded portion of the column, represents the reabsorbed fluid, all at the time indicated along the abscissa. The fine connected line represents the urinary volume in 15 x the scale of the columns. The EU per cent and the ECL per cent represent the percentage of the filtered urea and chloride that is excreted in the urine at the time of the simultaneous blood and urinary chemical studies. Note the increased FILTRATION.

Table 2

L. S., colored male, aged 50. Arteriosclerotic heart disease with congestive failure. April 5, 1932, creatinine 5 gr. at 8:20 a. m., and digalen I. V. 8 c. c. at 9:35 a. m., and digalen I. M. 12 c. c. at 9:40 a. m.

TIME	INT Interval in minutes	VOL Urinary output in c.c. volume	V Rate of flow per minute	$NaCl$ UX Urinary NaCl mg. per 100 c.c.	$NaCl$ SX Serum NaCl mg. per 100 c.c.	CO_2 Vol. per cent in serum	Ur UX Urinary urea mg. per 100 c.c.	Ur SX Serum urea mg. per 100 c.c.	Cr UX Creatinine in urine mg. per 100 c.c.	Cr. SX Creatinine in serum mg. per 100 c.c.	C Concentration index Cr. U % / Cr. S %	F Calculated glomerular filtration rate. C I U	R Calculated tubular reabsorption rate F-U	Fcl Glom. filtr. of NaCl $\frac{F \times Cl\ SX}{100}$	U Cl Urinary Exc. of NaCl $\frac{U \times Cl\ UX}{100}$	R Cl Reabsorp. of NaCl Fcl - Ucl.	ClR % Percent NaCl in R $\frac{R \times Cl}{R} \times 100$	$NaCl$ % Percent of Fcl exc. $\frac{Ucl}{Fcl} \times 100$	C Cl Concentration ratio of NaCl $\frac{Cl\ UX}{Cl\ SX}$ / $\frac{Cl\ SX}{Cl\ SX}$	F U Glom. filtr. of urea. $\frac{F \times U\ SX}{100}$	UU Urinary exc. of urea. $\frac{U \times V \times UX}{100}$	RU Reabsorbed Urea FU - UU	UR Percent urea in R $\frac{RU \times 100}{FU}$	RU Per cent of FU reab. $\frac{U\ R \times 100}{FU}$	CU Urea conc. ratio UU % / US %
U 6:00 -8:10 AM Bl 8:20 AM	130	53	0.41	428	462	59	1710	33.4	145	1.40	103.6	42.5	42.1	196	1.76	194.2	462	0.9	0.93	14.2	7.0	7.2	17.1	49.3	51.2
U 9:30 Bl 9:25	80	39	0.49	561	561	56	1090	42.8	630	3.16	199.4	97.7	97.5	548	2.75	545.2	561	0.5	1.0	41.8	5.34	36.5	37.5	12.8	25.5
U 10:35 Bl 10:30	65	22	0.34	428	428	60	1090	27.3	970	3.75	258.3	88.2	87.9	376	1.46	376.5	425	0.39	1.0	24.1	3.71	20.4	23.2	15.4	40.0
U 12:00 U 12:30 Bl 12:15	85 50 50	60 153	0.71 3.06	560 956	512	60	750 334	28.6	395 395	2.86	166.8 48.3	118.6 148	117.6 144.9	605 757	3.98 29.3	601. 747.	511 516	0.66 0.39	1.87	33.8 42.4	5.38 10.8	27.5 32.6	23.4 22.2	15.7 24.1	26.2 11.7
U 2:00 PM Bl 1:45	70	255	3.64	956	512	51	272	22.2	102	3.0	34	123.8	120.2	634	34.8	599.4	498	5.48	1.87	27.5	9.9	17.6	14.5	36.0	12.3
U 3:15 U 5:00 Bl 5:00	75 105 180	168 295 463	2.24 2.81 2.57	890 924	545	55	261 300	23.1	1022 105	2.61	40.2	103	100.4	562	20.0 23.9	536.1	535	4.62	1.7	23.8	5.85 8.44	15.4	14.8	35.4	13.0
U 7:30 U 7:30 Bl 8:20	150 60 210	375 130 505	2.50 2.17 2.40	999 660	545	53	300 355	23.1	117.7 126	2.61	45.0 48.3	112.5 104.5	110.0 102.1	614 572	25.0 14.3	533.7	540	2.5	1.2	24.2	7.5 7.7	16.5	16.1	31.8	15.1
U 8:30-2:30 U 2:30-8:30 Bl 8:30	360 360	500 100 680	1.39 0.50	748 297	462	59	375 545	25.0	222	1.87	119.	59.5	58.5	274	10.04 1.47	272.5	462	0.54	0.65	14.9	5.2 2.72	12.2	20.8	18.3	21.4

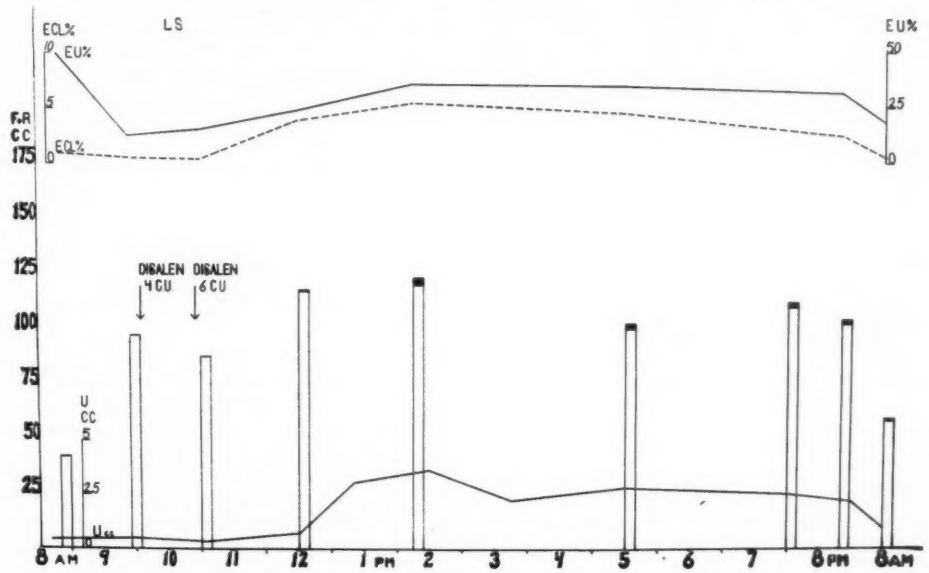

Fig. 2

(L. S.) Digalen diuresis. A chart similar to that shown in Fig. 1 representing the effects of digitalization by digalen intravenously (Clinical Chart No. 2, J.A.M.A.). The data for this chart are given in Table 2.

Table 3

P. C., colored male, aged 61. Syphilitic aortic regurgitation with congestive failure. March 1, 1932, creatinine 5 gr. at 7:00 a. m., and salyrgan 0.2 gr. I. V. at 9:25 a. m.

TIME	INT Interval in minutes.	VOL Urinary output in c.c. volume	U Rate of flow per minute	NaCl U% Urinary NaCl mg. per 100 c.c.	NaCl S% Serum NaCl mg. per 100 c.c.	Co_2 Vol. per cent in serum	Ur U% Urinary urea mg. per 100 c.c.	Ur S% Serum urea mg. per 100 c.c.	Cr U% Creatinine in urine mg. per 100 c.c.	Cr_s S% Creatinine in serum mg. per 100 c.c.	C Concentration index Cr U / Cr S%	F Calculated glomerular filtration rate C X U	R Calculated tubular reabsorption rate F-U	Fcl Glom.filtr. of NaCl F X $\frac{S}{100}$	UCl Urinary exc. of NaCl U X Cl U% $\frac{100}{100}$	R Cl Tub. Reabsorp. of NaCl Fcl - UCl	ClR Percent NaCl in R $\frac{R}{Cl} \times 100$	ECl Percent of FCl exc. $\frac{UCl}{Fcl} \times 100$	C Cl Concentration ratio of NaCl ClU% / ClS%	FU Glom. filtr. of urea F X $\frac{S}{100}$	UU Urinary exc. of urea U X U $\frac{100}{100}$	RU Reabsorbed urea FU - UU	Ur Percent urea in R $\frac{RU}{R} \times 100$	EU Percent of FU exc. $\frac{UU}{FU} \times 100$	Cu Urea Conc. ratio UU% / US%
U 6PM-6AM B1 7AM	720	210	.292	132	446	40	1200	23	259	1.67	155	45.2	44.9	59.6	.39	59.2	132	.65	.30	10.40	3.5	6.9	15.4	33.6	52.2
U 9:25 B1 9:25	205	56	.273	99	462	42	1330	21.4	400	3.0	123	36.3	36.0	35.9	.27	35.6	99	.75	.21	7.77	3.55	4.22	11.7	45.7	62.1
U 11:25 B1 11:25	115	92	.80	264	412	32	500	24.0	228	2.61	87.5	70.0	69.2	185.	2.11	182.9	264	1.14	.64	16.80	4.0	12.8	18.5	23.8	20.8
U 1:10 PM B1 1:15	110	216	1.96	560	462	31	480	30.0	84.	2.14	39.2	76.8	74.8	430	11.0	419	560.	2.56	1.21	23.2	9.4	13.8	18.5	40.5	16.0
U 2:10 B1 2:10	60	180	3.00	924	462	36	141	30.0	56.6	2.07	27.4	82.2	79.2	758	27.8	730.2	922	3.66	2.0	24.7	4.2	20.5	25.9	17.1	4.7
U 3:25 B1 3:15	75	190	2.54	528	412	40	120	23.0	51	2.21	22.1	56.2	53.6	299	13.4	285.6	532	4.47	1.28	12.9	3.0	9.9	18.5	23.2	5.2
U 4:10 B1 4:15	45	78	1.73	561	412	43	133	33.4	85	2.31	28.1	48.7	46.0	273	9.7	263.3	573	3.55	1.36	16.5	2.3	14.2	3.09	13.9	3.98
U 5:15 B1 5:10	65	232	3.57	561	446	48	172	28.6	56	2.50	22.4	80.0	76.4	449	20.0	429	564	4.46	1.26	22.9	6.1	16.8	22.0	26.8	6.01
U 6:10 B1 6:10	55	78	1.43	528	430	47	150	27.3	65	2,66	22,7	32.2	30.8	170	7.5	162.5	527	4.40	1.23	8.6	2.13	6.7	21.7	24.2	5.5
U 6PM-6AM B1 9AM	720	1190	1.65	396	462	41	120	27.3	445	2.31	19.25	31.8	30.2	126	6.53	119.5	399	5.18	.86	5.7	1.98	6.7	22.3	22.8	4.4

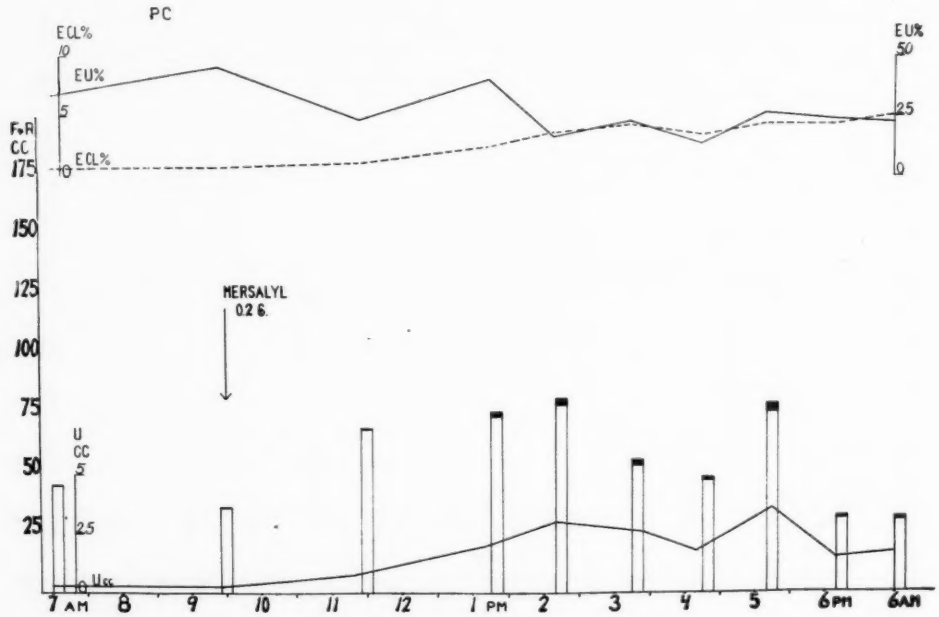

Fig. 3

A filtration reabsorption chart of the data on P. C. given in Table 3. Note that there is little, if any, increase in glomerular filtration per minute, but a striking decrease in reabsorption, to account for the diuresis.

ally be given at frequent intervals over a period of many months, but now and then renal injury results. The pathologist has twice demonstrated to us unmistakable evidences of tubular degeneration, presumably a salyrgan effect, in patients to whom the drug was repeatedly administered. These observations stress the need for studies of renal function both before and during the use of salyrgan, especially where its frequent use is required.

Salyrgan.—Salyrgan is best given intravenously in doses of 1.5 to 3 grains (0.1 to 0.2 gram). In administering the drug in this manner it is desirable to withdraw into the syringe an amount of blood at least equal to the volume of the fluid in which the salyrgan is dissolved preliminary to the injection. This is done in order to obviate the possibility of venous thrombosis. In contrast to theophylline ethylene diamine, the intravenous injection of salyrgan is somewhat slower in inaugurating diuresis. In a large series of studies now in progress, the average time of onset has been 2 to 3 hours, with the maximum of about 7.5 c. c. per minute reached in 5 to 6 hours. The effect usually persisted for a longer period than after other diuretics, and not infrequently the diuresis was maintained into the second 12-hour period, or even into the second day. A strikingly different mechanism of diuresis was also observed when salyrgan was administered. In patients with congestive heart failure, detailed studies by the Rehberg method showed only a slight rise in filtration during salyrgan diuresis, but a conspicuous decrease in tubular reabsorption, in contrast to the augmented glomerular filtration following theophylline ethylene diamine (*Fig. 3*).

THE COMBINED USE OF MERCURIAL AND XANTHINE DIURETICS

On the basis of our conception of the divergent mechanism by which diuresis is accomplished, namely, predominant increase in glomerular filtration in the xanthines, and primarily defective tubular reabsorption in the mercurials, the theory of different action has been put repeatedly to clinical test. After the 3-day rest period, theophylline ethylene diamine was administered, and when the base line was again reached, a second diuresis was induced by salyrgan. Then, so soon as the urinary output dropped to the low pre-diuretic level another injection of theophylline ethylene diamine was given, and almost invariably the third outpouring of urine was definitely greater than either of the two previously obtained (*Fig. 4*). This augmentation occurred in spite of the fact that the patient had had two previous periods of profuse diuresis and had, consequently, lost many pounds of edema. This, it is believed, would counteract any possible salutary effect of decreased kidney congestion, of the probable improvement in coronary circulation, resulting from theophylline vasodilation, as well as that of the added bed rest.

SALYRGAN AND AMMONIUM CHLORIDE

Ammonium chloride in large doses, one and one-half to two drams (6.0 to 8.0 grams) daily is a diuretic of variable and uncertain action. It is thought that its effect is produced by the acidosis which follows its administration. Usually the best results have been obtained when it is given to patients who are on a salt-poor diet, and in whom the fluids are restricted to 1,000 to 1,500 c. c. per 24-hour period. Keith, Barrier and Whelan[7] showed that patients who had been given massive doses of ammonium chloride for several days often had a profuse diuresis when novasurol was administered, even though neither drug singly was effective. This combined effect of ammonium chloride and novasurol can be duplicated by using salyrgan instead of novasurol, and a more marked diuresis has frequently been observed when salyrgan was given after preliminary ammonium chloride therapy than when salyrgan alone was administered. The result of this treatment is at times very dramatic in its effect on patients refractory to other diuretics. Ammonium nitrate is of equal value with ammonium chloride and is preferred by some because it is somewhat more easily borne by the stomach.

The exact mechanism by which the combined action of an acid salt with a mercurial is effected is not clear and presents an interesting problem for future study. Blumgart[8] believes that it is a pure summation of the action of the two drugs, each of which possesses definite diuretic properties.

OTHER DIURETICS

Within the last few years certain water soluble bismuth salts, especially sodium tetrabismuth tartrate, have been reported by Mehrtens, Hanzlik, *et al.*,[9] and Stockton[10] to have definite diuretic effect, and to be preferable largely because of persistence of action and lack of toxicity. The intramuscular method of administration, which is alleged to be effective in the case of bismuth, is considered an added advantage. The various salts of bismuth, including the insoluble, oil soluble and water soluble prepara-

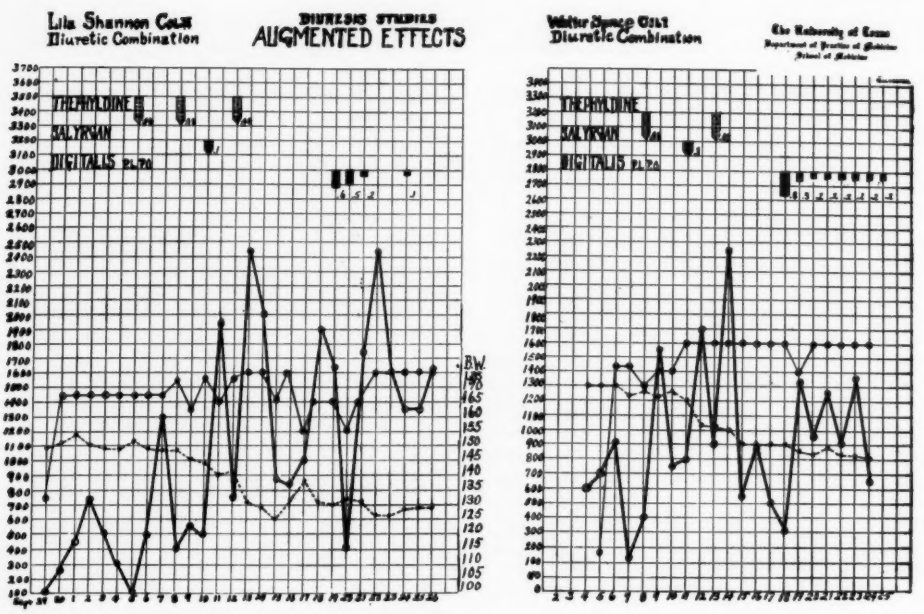

Fig. 4

Charts showing the striking combination effects of using salyrgan for its tubular effect followed by theophylline for its glomerular effect. A preceding theophylline ethylene diamine injection serves as a control. Urine output represented by o—o (circle connected by heavy line), body weight by o - - - o (circle connected by broken line), and fluid intake by o—o (circle with dot connected by light line). Thephyldine and salyrgan were given intravenously; powdered leaf digitalis was administered *per os*.

tions, have been used. These have been administered under the most promising therapeutic conditions as the first drug following the three-day control period of rest, and as the only drug over a prolonged period of observation in some instances. Occasionally bismuth was used during and after digitalization. The results, as a whole, have been very disappointing even in congestive heart failure accompanying syphilitic heart disease. In only one instance was it possible to accomplish anything that could be compared with the diuresis obtained with other drugs, and in this case the insoluble potassium bismuth tartrate in very small doses was moderately effective. Apparently the mode of action of bismuth, when it is successful, is similar to that of mercury, namely, increased output of fluid as a result of decreased tubular reabsorption. Just as in the case of the mercurials, it may well be that bismuth prepared especially for intravenous injection might be expected to induce a more spectacular diuresis than is produced by the same drug administered intramuscularly. In our experience it is worthy of note that the edema refractory to intramuscular bismuth responded promptly to the other anti-edemic drugs.

UREA

Urea has been employed as a means of dissipating abnormally accumulated tissue fluid, especially when ascites predominated in the clinical picture. To be effective, it must be administered in massive doses, but even in amounts of one to two ounces (30 to 60 grams) it is apparently non-toxic. It is usually given by mouth in 25 to 50 per cent aqueous solution, which may be flavored with fruit juices. The greatest advantage of urea is that it may be given over a long period, even two or three years, without detrimental effect, provided there is no renal insufficiency. It is most effective when edema is marked, and decreasingly so as the edema subsides, but it seems to maintain the cardiac cripple who has a tendency to congestive failure in satisfactory water equilibrium. The information at hand suggests that diuresis is probably accomplished by the filtration of increased amounts of urea, a low threshold substance, and therefore the consequent transport

with it through the kidney of large amounts of water.

PARATHYROID HORMONE

Parathyroid hormone has been advocated as a diuretic in the refractory edema of chronic nephritis and nephrosis. Its action is very imperfectly understood, but it is believed to be associated in some way with calcium mobilization. This is emphasized by the finding of a low blood calcium in some patients who have responded favorably to its use. A most dramatic diuretic response has been obtained in a resistant edema in a patient with congestive failure complicating rheumatic heart disease with mitral stenosis. This experience certainly warrants further trial and investigation of the mechanism by which the results are accomplished, and the conditions under which favorable action might be expected.

THYROID EXTRACT

Thyroid extract has a limited field of usefulness in the congestive heart failure of severe myxedema. Here again the mode of action of the drug has not been definitely determined, but it appears likely that the diuresis is dependent upon the improved myocardial function with resulting augmentation of general circulatory efficiency. The heart in the myxedematous patient has been repeatedly shown to decrease markedly in size under adequate treatment with thyroid extract, and upon this basis there probably rests sufficient explanation for the improved blood flow. In a case of severe myxedema of nine years' duration, with general anasarca, a prompt and prolonged diuresis followed the administration of thyroid extract, with a loss of weight of 29 pounds in fifteen days. Once such an edema is removed, it does not tend to reaccumulate so long as sufficient thyroid extract is administered to maintain a normal basal metabolic rate.

SUMMARY AND CONCLUSIONS

The significance of edema as a symptom in congestive heart failure and the impediment which it offers to the recovery of myocardial and circulatory equilibrium is discussed and emphasized.

All forms of diuretic drug therapy should be used when indicated as adjuvants to complete bed rest and digitalization which alone, in many instances, are capable of restoring myocardial efficiency with a resulting profuse diuresis.

Theophylline ethylene diamine, administered intravenously, is the most efficacious of the xanthine group and probably the safest of all the powerful diuretics. Diuresis is accomplished in this group by an increase in glomerular filtration with a concomitant slight decrease in tubular reabsorption. The average time of onset, the height, and the duration of the diuresis are stated.

Salyrgan is the mercurial diuretic of choice. Augmentation of urinary flow is effected by only a slight rise in filtration with a conspicuous decrease in tubular reabsorption. In contrast to theophylline its action is less prompt, but more pronounced and prolonged.

On the basis of the different action of the mercurial and xanthine diuretics, the rationale of their combined use is brought forward and discussed.

Ammonium chloride or ammonium nitrate used in conjunction with salyrgan frequently produces a more marked diuresis than salyrgan alone. The exact method whereby this is accomplished is not yet known.

In our experience, the diuretic action of the various bismuth salts has been quite uncertain. Success was obtained in only one instance. Further study of the effect of bismuth given intravenously is suggested.

The indications for the less commonly used diuretics, urea, parathormone and thyroid extract and the expected results are briefly discussed.

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DISCUSSION (*Abstract*)

Dr. W. B. Porter, Richmond, Va.—Dr. Stone and his associates have presented in a workable form their conclusions in the treatment of cardiac edema. Their observations are confirmatory of the rationale and justification of the regimen which has become standardized in this country, England and on the continent.

The only grievance which I have with Dr. Stone's conclusion is that the entire emphasis is given to the action of the various remedies on renal function with no consideration for their effect upon the extrarenal

factors which have operated in the production of the edema.

We know that digitalis modifies the circulation throughout the body and that there is much evidence that the theobromin diuretics act not only on the vessels leading to the glomeruli, but a'so on the vascular bed throughout the body. It is suggested therefore that one must consider the subject rather broadly if he is to draw any conclusions as to the nature of the modus operandi of these drugs used in the treatment of congestive heart failure.

MALARIA TREATMENT OF DEMENTIA PARALYTICA*

RESULTS IN 205 CASES AFTER FIVE TO ELEVEN YEARS

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Malaria treatment of dementia paralytica was introduced into this country at Saint Elizabeth's Hospital in December, 1922, and up to the end of 1928, 208 cases had been successfully inoculated with benign tertian malaria. It may be well to mention that these cases were unselected consecutive admissions. Three of them are excluded from further consideration because they were cases of juvenile paresis. We have been able to follow up 195 of these patients for five or more years, and this paper represents the critical evaluation of the results to date.

There has been almost universal acceptance of the value of malaria in the treatment of dementia paralytica. In general it is believed that about 30 per cent of the patients develop a satisfactory remission; that another 30 per cent are improved, while 30 per cent remain unchanged and 10 per cent die within a year or two. Recently, however, a number of communications have appeared tending to show that the remissions obtained are not lasting, and that with the passage of time the number of improved cases falls rather rapidly. Indeed, Buscaino[1] is quite pessimistic when he says:

"From present experience the conclusion is reached that malaria does nothing else, even in the most favorable cases, than prolong for a few years the social life of patients with incipient or confirmed general paralysis."

Buscaino's conclusions are based upon his own twenty cases. The immediate results were 65 per cent improved or well, while after four and a half years only 25 per cent could be considered improved and 50 per cent were known to be dead. Series of cases have also been reported by Dattner,[2] Kirschbaum,[3] Reid,[4a] and Stanley.[5] Dattner, for instance, in 129 cases followed over a period of six to eight years, found 40 per cent improved and 47 per cent dead; Kirschbaum had good immediate results in 68 per cent, but after ten or twelve years the percentage had fallen to 34, while Reid, in his first four series of 99 cases, followed for more than five years, found only 15 per cent improved, while 65 per cent were dead. Stanley's figures are 37 per cent improved and 41.4 per cent dead in the early stages, and 22 per cent improved and 51 per cent dead after a period of from three to seven years in a group of 161 cases which could be traced.

If the malaria treatment is useful only to prolong life, it does not answer the requirements of either physician or patient, and if relapses occur or deterioration progresses in spite of treatment, very little is gained from the social point of view. Our own results, however, are not in accord with those mentioned above, with the exception of Dattner's. The present condition of the patients is shown in *Tables 1* and *2*. All of these patients, 205 in number, have been followed for a period of five or more years with the exception of 10 that have been untraced, and most of them have been under observation in Saint Elizabeth's Hospital or in some other hospital, or have been reached through corre-

Table 1

PRESENT STATUS OF CASES TREATED FROM FIVE TO ELEVEN YEARS AGO: 205 PATIENTS

Living	Dead	Unknown
138	57	10
67.3 per cent	27.8 per cent	4.9 per cent

Table 2

STATUS OF 138 LIVING PATIENTS

Discharged; regularly employed at occupation equivalent to former.	Discharged; employed at some occupation	Discharged. Not employed	Still in some hospital; parole and working privilege	Still in hospital, confined to wards
31	11	20	25	51
22.4%	8.0%	14.5%	18.0%	37.0%

*Read in Section on Neurology and Psychiatry, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

*From St. Elizabeth's Hospital, Washington.

spondence with friends and relatives, and by means of personal contact, within the last few months. Moreover, it appears from our studies that, except in the deteriorated cases, there has been relatively little change during the past several years, indicating that a definite arrest of the disease process has taken place, and that the patient is functioning at a level determined by the severity of the permanent cerebral damage sustained before the treatment was administered. The deteriorated cases represent a considerable percentage of the living group, but they show certain peculiar features that will be discussed later.

For purposes of evaluating the results of therapeutic malaria we have used a classification based upon the social behavior of the patient. Nevertheless, it must be admitted that in many instances the economic status of our patients has been influenced by pension and disability payments to veterans by the United States Government. Were it not for this source of income, some patients would now be public charges, probably in some mental hospital, on account of certain peculiarities of behavior. On the other hand, the present period of economic stress has undoubtedly prevented certain capable patients from securing employment. The present classification, therefore, represents a cross-section of the patient's social existence at the latest period of record.

Group I.—These are patients discharged from the hospital regularly employed at an occupation equivalent to the former one. There are 31 in this group. They may be considered, to all intents and purposes, as recovered. Where their economic status has been altered by fortuitous circumstances, due allowance has been made. For instance, one veteran worked for seventeen months in a responsible position, but was discharged when his employers were notified of the previous psychosis. Shortly thereafter, his governmental disability allowance was terminated. Certain individuals have made an even better adaptation, taking on new responsibilities, earning higher salaries than they were before hospitalization. One young woman, when interviewed by the social worker, was found to have been successfully married, to have had two healthy children and to be pregnant with the third. She was evidently making an excellent domestic adjustment. In talking with patients of this class it is difficult to detect anything abnormal either mentally or neurologically, and they could pass as first rate citizens.

Group II.—These are patients discharged from the hospital and employed at some occupation, even if irregular. The narrow zone between regular employment and none is occupied by 11 individuals. From our correspondence with them and their families it seems quite evident that they have sustained some permanent damage, which appears either as lack of ambition or irritability or restlessness that interferes with satisfactory employment. Possibly as the demand for labor increases this group will enlarge due to accessions from *Group III,* but permanent employment of these individuals at any exacting task will probably be impossible.

Group III.—These are patients discharged from the hospital, but not employed. There are 20 patients in this group. They are able to get along outside the hospital, but are supported by their families or their pensions, or they are living in soldiers' homes in various parts of the country. It is interesting to note the number of fishermen in this group. Letters come back from the families of these men indicating that they are occasionally moody and impatient. Sometimes more serious difficulties arise so that the families would be glad to return the patients to the hospital. On the whole, however, we feel that the hospital has made no mistake in discharging them. Some of the discharges, indeed, followed unauthorized absence of the patient from the hospital.

Group IV.—These are patients still remaining in this or another hospital, but enjoying parole or working privileges. These patients have deteriorated too much to be trusted with discharge, although, in some cases, were domestic surroundings favorable, they could be allowed to go home. Irritability and erroneous judgment are the principal reasons for their continued hospitalization. They often make satisfactory workers at the simpler hospital tasks. As a general rule, however, they represent rather high types of individuals who have suffered serious mental deterioration and yet have not the physique or aptitude for manual labor. Hence they remain protected, carrying on their tasks, instead of being sent back to their homes to be hewers of wood and drawers of water. There are 25 patients in this group.

Group V.—These are patients confined to their wards. These 51 patients were deteriorated already, and many of them show gradual further slipping from year to year. Among themselves they vary greatly. Some are assaultive, others are mute, a few are completely demented, but most of them are quiet, rather slovenly in appearance, with well-marked neuro-

logical stigmata. They sit around the ward, doing no work beyond pushing a floor mop and eating their three meals a day in the steady routine of the common denominator of the chronic patient.

DECEASED PATIENTS

Fifty-seven, or 28 per cent, of the 205 patients originally treated are known to be dead. This is a considerably lower percentage than that recorded even by Dattner's 47 per cent, and far below the 65 per cent reported by Reid. Some of the deaths were due to intercurrent diseases and more of these may be anticipated. Deaths during the malaria treatment occurred in 11 cases and 28 more died within three years. Only four of these patients could be classed as improved, so that it is evident either that the malaria had little or no effect in arresting the paretic process or that the advanced condition of the patient at the time malaria was inoculated offered little hope of improvement. In ten instances death was due primarily to neurosyphilis, but four instances of pulmonary tuberculosis and several instances of visceral syphilis helped to swell the total. Of nineteen patients dying more than six months after malaria and coming to necropsy, only four showed persistent inflammatory manifestations of dementia paralytica. The persistence of syphilitic lesions of the viscera with clearing up of the inflammatory manifestations in the brain has an important bearing upon the modus operandi of the therapeutic malaria, as indicated in a previous paper by one of us.[6]

There is no need of stressing the pathologic findings in the brain in treated cases, since they have been described in many articles. Suffice it to say that in most instances the inflammatory lesions disappear, while the degeneration, atrophy and sclerosis persist, so that the picture of stationary paresis results.

SEROLOGICAL STUDIES

Reid[4b] has made a comprehensive study of the sera in patients treated by malaria and our findings bear out his conclusions with the exception that in our experience the gold reaction, rather than the Wassermann, is usually the last to become negative, while the globulin and cell count subside quickly. Improvement in the reactions may be noted during the first six months, but in many instances it is five years or more before the last vestige of reaction disappears. In the study of the serological status in 113 cases five or more years after malaria a high percentage of negative spinal fluids was encountered. Most of these fluids, indeed, came from patients who were confined to their wards and markedly deteriorated, so that the presence of a normal fluid does not by any means indicate a clinical remission. On the other hand, a persistently positive spinal fluid is a good indication that the process has not been terminated and that deterioration will progress. In no case discharged from the hospital has the fluid remained positive after five years. Our findings are given in *Table 3*. A positive Wassermann reaction is taken arbitrarily as a Kolmer reaction of 4-0-0-0-0 or greater, while a positive colloidal gold reaction has one or more 3's in it.

Table 3

CORRELATION OF CLINICAL AND SEROLOGICAL STATUS OF 113 CASES

Serology	Disch.; reg. emp. same occup.	Disch.; employed at some occupation	Discharged; not employed	In hospital; parole and working	In hospital; confined to wards	Dead
Negative	9	5	5	14	27	3
Wass. pos. / Gold neg.	0	0	2	2	6	0
Wass. neg. / Gold pos.	5	0	3	2	6	1
Positive	0	0	0	4	9	10

NEUROLOGICAL STUDIES

We have recently reviewed all the patients still remaining in the hospital. All of them were carefully studied before the induction of malaria, so that comparison may be made. In a few instances some improvement has been noted, whether in the reactivity of the pupils or in the decrease of exaggerated reflexes. Only rarely has a lost tendon reflex returned. On the other hand, in the deteriorating group of patients, further progression is evidenced by complete rigidity of the pupils, exaggerated tremors of the lips and tongue or loss of tendon reflexes. On the whole, the neurological manifestations show the least alterations of any. This is, indeed, not surprising, since these phenomena depend upon injury to subcortical centers, where substitution and compensation are much less apt to take place than at the cortical level.

PSYCHIATRIC STUDIES

The 54 patients (48 men and 6 women) remaining in Saint Elizabeth's Hospital show varying degrees of mental reduction and the great

majority of them are of the simple deteriorated type, with some dullness, defects in judgment, memory and orientation, and lack of insight outstanding. Incoherence or mutism is prominent in the markedly deteriorated cases which comprise one-third of the group. Delusions and hallucinations are observed in very few instances and even then it is exceptional for the patient to react to them strikingly. Grandiosity is present in only three cases, although there is a previous history of this symptom in several others. More surprising is the paucity of hypochondriacal attitudes or somatic delusions. In most of the cases the emotional reaction is that of contented indifference, but in others there are flurries of irritability. The behavior problem with two of the markedly deteriorated patients is less to the extent that they are no longer assaultive, but five others (including three women) continue to show assaultiveness at times. None of the entire group is bed-ridden, and, indeed, the general physical condition (including the body weight) of the group as a whole is remarkably good. This is in keeping with the observations of Reid[4a] and of Warner.[7] Certain of the patients give a suggestion of mummification in their appearance, possibly associated with an arrested paretic process.

IMMEDIATE AND REMOTE RESULTS

The first study of our malaria-treated cases was done in 1925 upon 55 patients observed over a period of two years. At that time one of us[8] formulated the results according to the following table. A comparison of the present status of a larger number of patients with the earlier estimation probably indicates better than anything else the permanent value of the malaria treatment.

	1925		1933	
	No.	Per Cent	No.	Per Cent
Improved	18	33	62	30
Unimproved	28	51	76	37
Died	9	16	57	28
Untraced	0	0	10	5

It is striking to note that the percentage of improved has been maintained during the passage of years, and this coincides with Dattner's[2] experience.

THE IMPORTANCE OF EARLY TREATMENT

The effectiveness of malaria in securing a permanent arrest of the paretic process in most instances seems fairly well established in the foregoing study. A further point that we wish to emphasize is the importance of early treatment. The patients reported upon in this study have all been hospital cases duly recognized and usually adjudicated. Hence, in many respects, they represent clearly defined and often advanced cases. Even so, 30 per cent are able to go back to their homes and make some sort of adjustment. We believe that if all the patients could have had the advantage of early treatment, the number of recoveries could be at least doubled.

Table 4

PRESENT STATUS OF PATIENTS CLASSIFIED ACCORDING TO DURATION OF PARESIS BEFORE TREATMENT

	Less than 1 Year Per Cent	One to Three Years Per Cent	More Than 3 Years Per Cent
Discharged	59	19	9
Transferred	14	21	14
In hospital	20	33	38
Dead	7	27	39

In *Table 4* is an analysis of our cases classified with regard to the duration of their mental symptoms before the administration of malaria. It can readily be seen that treatment within a year after the onset of mental symptoms offers a much better prognosis than does delayed treatment. This is further borne out by the experience of numerous individuals in treating patients before the period when it became necessary to commit them to mental hospitals. Results as high as 67 per cent at full working capacity have been reported.[6b]

INFLUENCE OF THE NUMBER OF PAROXYSMS

There has been some disagreement as to the number of malaria paroxysms necessary to secure a satisfactory arrest, and indeed some papers have appeared indicating that no fever at all is necessary. However, our findings in *Table 5*

Table 5

RESULT OF TREATMENT, CLASSIFIED ACCORDING TO NUMBER OF PAROXYSMS

Status	Less than Ten Paroxysms		Ten or More Paroxysms	
	No.	Per Ct.	No.	Per Ct.
Discharged. Employed occup. equivalent of former one	1	2.3	29	20.
Discharged. Employed at some occupation	1	2.3	10	3.8
Discharged. Not employed	1	2.3	16	11.
Still in hospital. Parole and working privileges	6	14.	18	12.3
Still in hospital. Confined to wards	11	25.7	39	29.7
Dead	23	53.4	34	23.2
Present status unknown	1	—	15	—

Cases of unknown status are not included in per cent calculations.

indicate that the number of paroxysms shows a high correlation with the number of altogether satisfactory results. For instance, of 43 patients who experienced less than ten paroxysms only one (2 per cent) is self-sustaining; whereas, in a group of 146 patients who had ten or more paroxysms, 29 (20 per cent) are in full remission and carried in *Group I.* Moreover, of the 43 patients who had less than ten chills, 53 per cent are dead; whereas, in the second group only 23 per cent have died. It was the policy of this hospital, early in its experience, to subject the patients to as many paroxysms as they could tolerate and some examples of as many as twenty paroxysms have been noted. More recently, influenced largely by reports from the German literature, the number of paroxysms has been reduced to not more than ten. We propose, however, in the future handling of our paretics to return to our original policy of permitting them to have as many paroxysms as they can safely tolerate.

SUMMARY

One hundred and ninety-five out of a total of 205 cases of dementia paralytica were followed for a period of from five to eleven years after they received malaria treatment. Of those traced, 31 per cent are discharged from the hospital, 39 per cent remain hospitalized, and 30 per cent are known to be dead. The remissions obtained show indications of being permanent and the percentage of recoveries has not declined notably with the passage of years.

Failures in malaria therapy are chargeable largely to delay in its administration and to restriction of the number of paroxysms.

Persistently positive serologic responses after three years indicate the probability of failure, but negative responses are often found in deteriorated patients.

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TRAUMATIC SHOCK AND HEMORRHAGE*

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The following description of the clinical picture of shock was given by Samuel D. Gross[1] in 1872:

"The person, although severely injured, congratulates himself upon having made an excellent escape, and imagines that he is not only in no danger, but that he will soon be about again; in fact, to look at him, one would hardly suppose, at first sight, that there was anything serious the matter; the countenance appears well, the breathing is good, the pulse is but little affected, except that it is too soft and frequent, and the mind, calm and collected, possesses its wonted vigor, the patient asking and answering questions very much as in health. But a more careful examination soon serves to show that deep mischief is lurking in the system; that the machinery of life has been rudely unhinged, and that the whole system is profoundly shocked; in a word, that the nervous fluid has been exhausted and that there is not enough power in the constitution to reproduce and maintain it. The skin of such a person assumes an icteroid, or sallow, cadaverous appearance, feeling at the same time doughy and inelastic; the extremities are deadly cold; the pulse makes a desperate effort at reaction, but is, at best, weak and tranquil for one who has sustained such an amount of violence. The system does not seem to be conscious of what has occurred; its sensibilities are blunted, and it is incapable of suffering. Nature, to use the language of Hunter, does not feel the injury."

There have been advances in our knowledge concerning the mechanism of the production of shock since 1870, but this description of the clinical picture by Gross could not be improved upon at the present time. Severe physical injury is frequently followed by a low or declining arterial pressure, a low venous pressure, a rapid, weak pulse, a diminished blood volume, a normal or increased red blood cell count, a subnormal temperature, a lowered metabolism, a cold, moist skin, sweating, thirst and often nausea and vomiting.

Many theories have been offered in an effort to explain shock. Most of these have been directed towards discovering the reason for the lowered arterial pressure. Many of the earlier

*Read in Section on Surgery, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

*From the Department of Surgery, Vanderbilt University.

writers attributed it to some disturbance brought about through the nervous system. This disturbance supposedly resulted in vasomotor paralysis, or exhaustion of the vasomotor center, or inhibition of all the functions of the body, or direct effects upon the heart. The ideas of the earlier students of the subject are not so erroneous as they might appear to be on first examination, for many of them were referring to what is known today as primary shock or collapse. Primary shock in its present usage refers to the state of collapse which appears almost immediately following the receipt of an injury. The term is used in contrast to secondary shock in which the interval separating the injury and the marked decline in pressure is usually an hour or longer. Primary shock is neurogenic in origin. The mechanism of the production of the condition seems to have been satisfactorily explained by Goltz[2] in 1863, when he found that the striking of the viscera of the frog was associated with a reflex inhibition of the heart through the vagus and a lessening of vascular tone throughout the body and particularly in the splanchnic area.

It has been in an effort to explain secondary or delayed shock that most of the theories have been offered. These include the theory of fat embolism, of acidosis, of acapnia, of suprarenal hyperactivity and hypoactivity, of inhibition, of vasomotor exhaustion and of toxemia. Several of these theories have become untenable, since it seems to have been definitely proven that secondary or traumatic shock is associated with a diminution in the volume of blood and with vasoconstriction which is replaced by vasodilatation only during the terminal stages. The theory which has had the most supporters during the past fifteen years is the one which maintains that shock following trauma is due to the absorption of toxic products which result from the injury to the tissues. This theory is founded upon clinical observations and experimental findings. Probably the most significant experiments are those that were performed by Cannon and Bayliss,[3] in which they produced shock in anesthetized cats by striking one of the posterior extremities many blows with a hammer. Death resulted usually after an interval of several hours. They then determined the amount of blood and lymph that had been lost into the injured area by weighing the two posterior extremities after amputations had been performed by symmetrical cuts across the upper thighs. It was found that there was not a sufficient difference in weight to account for the death by the loss of blood and lymph alone. The possible effects of nervous impulses were eliminated by sectioning the spinal cord in some of their experiments. It was concluded that the low blood pressure resulting from the trauma was due not to loss of blood into the injured area, nor to fat embolism, nor to the effects on the nervous system nor to over-ventilation, but to the passage of toxic products from the injured area into the general circulation. The toxic products were believed to be histamine or some closely related substance.

Using deeply anesthetized dogs instead of cats, I repeated the experiments of Cannon and Bayliss. It was observed[4] that trauma to the thigh was associated with swelling which extended into the loose tissues of the groin and flank. Hence, it was believed that the amputations had not been performed at a sufficiently high level in the experiments of Cannon and Bayliss if the entire loss of blood were to be determined. Therefore, the amputations were performed above the level to which the swelling extended in my experiments and it was found that there was a loss of a sufficient part of the blood volume into the injured area to account by itself alone for the decline in blood pressure. This loss equaled approximately one-half of the total blood volume. In other experiments, shock was produced by traumatizing an extremity which had its venous and lymph channels completely occluded in order that there could be no possibility of the absorption of toxic products, and it was found that there was a sufficient loss of fluid into the injured extremity to cause the decline in blood pressure. Similar results were obtained by Parsons and Phemister.[5]

It was noted in my experiments that trauma to an extremity usually resulted in an increase in the concentration of the red blood cells in the blood stream. This increase in concentration was due in part at least to the fact that the fluid that was lost into the injured area consisted of a larger proportion of plasma and a smaller proportion of red blood cells than were present in the blood stream. It is well known that shock following trauma in patients is usually associated with an increase in the concentration of the blood.

It seemed from these and from other experiments that in animals shock could be produced that was closely similar if not identical to that observed in patients, and that the loss of plasma and of red blood cells at the site of injury only was sufficient to explain the decline in blood pressure. If these observations are correct, then one may ask why it is that the criteria

of hemorrhage and of shock are not identical. The most important and perhaps the most generally accepted distinctive characteristics of shock and of hemorrhage are as follows: first, shock is associated with an increase in the concentration of the red blood cells, while hemorrhage results in a dilution; second, the transfusion of blood to patients in shock frequently exerts no permanent beneficial effect, while the condition resulting from hemorrhage is greatly aided by transfusion; third, the tissues of the body show capillary dilatation and congestion and petechial hemorrhages following death from shock. Following death from hemorrhage, the tissues present an anemic appearance. I think that this difference in the characteristics of shock and hemorrhage is explained by the following experimental and clinical observations.

The results obtained in the previous studies of traumatic shock so clearly indicated that this condition could be attributed solely to the loss of approximately one-half of the blood volume into the injured area, that it seemed reasonable to believe that the same types of alterations could be produced by hemorrhage alone. For the purpose of this study, the method of producing death by the removal of blood was somewhat different from that usually employed. Blood was withdrawn in such manner that the alterations in the blood pressure were closely similar to those that were observed in the experiments in which trauma was produced. Pain was prevented by the injection of procaine hydrochloride at the sites where cannulae were introduced into the blood vessels. Blood was withdrawn in small amounts at frequent intervals until the blood pressure declined to approximately 70 mm. Hg. If the pressure rose, additional blood was removed. After a sustained depression of this degree in the blood pressure had been produced, the animal was allowed to die without the further removal of blood. Usually death occurred approximately an hour after a marked sustained reduction in the blood pressure had been caused. An increase in the concentration of the red blood cells occurred in some of the experiments. Capillary congestion and dilatation and petechial hemorrhages were observed in some of the organs. Blood stained material was present in the lumen of the intestinal tract in most of the experiments.

For the purpose of studying the effects of a low blood pressure of longer duration resulting from hemorrhage, other experiments were performed in which death was delayed by the transfusion of blood from a suitable donor. By combining the removal of blood in order to reduce the blood pressure, with the introduction of blood when death seemed to be imminent, the blood pressure was maintained at a low level for approximately three hours. No reaction as a result of the introduction of blood was observed. All of the animals died despite the fact that slightly more blood was introduced than was removed. An increase in the concentration of the red blood cells was observed in all experiments. Capillary congestion and dilatation, hemorrhage and some necrosis of cells were present in the tissues following death.

Thus it is to be observed that an increase in the concentration of the blood, a failure to respond favorably to the transfusion of blood and alterations in the tissues, are not characteristics that are peculiar to traumatic shock since it is possible to produce them by hemorrhage.

In the care of patients, one rarely encounters as a result of hemorrhage a low blood pressure that persists for several hours. If bleeding from a large blood vessel takes place, usually either early death occurs or the loss of blood is stopped and recovery follows. If the bleeding results in almost immediate death, an anemic appearance of the tissues is found at autopsy. If the bleeding is controlled, usually the remaining volume of blood is augmented by the passage of fluids from the tissue spaces into the blood stream or fluid is added artificially, and a rise in the blood pressure and a decrease in the concentration of the blood occur. A somewhat different set of conditions is encountered when fluid is lost from many small vessels into an injured part. The speed with which fluid leaves the blood vessels is usually slower because of the small size of the vessels and because of the pressure in the tissue spaces. As the pressure in the blood vessels diminishes and the pressure in the tissue spaces increases, the loss of fluid locally is still further retarded. The fluid that is lost has a larger proportion of plasma and a smaller proportion of red blood cells than that existing in the blood stream. This accounts partially for the increase in the concentration of the blood. Since the blood pressure usually remains at a low point for a considerable time preceding death following trauma to large masses of muscle, the tissues of the body are partially deprived of blood and oxygen and alterations such as capillary congestion and dilatation and hemorrhage take place.

These observations explain why the treatment of severe shock is unsatisfactory. After damage

has resulted from an inadequate supply of blood to the tissues for a considerable time, regardless of the cause, fluids introduced into the blood stream will escape.

There may be various contributory factors which are partially responsible for the production and maintenance of shock. Food and water deprivation and exposure to cold increase the ease with which it can be produced. Prolonged anesthesia may greatly exaggerate the condition. Serious illness reduces one's ability to withstand the loss of blood and to tolerate trauma.

It is to be emphasized that this paper is concerned in the main with the condition that develops as a result of the slow loss of blood or following trauma to large masses of muscle. If the experiments have been correctly interpreted, it seems that the diminution in the blood volume as a result of the local loss of fluid from the blood stream following injury to muscles is responsible for the decline in blood pressure and shock. The early alterations are the important ones. After the condition is fully developed, many changes take place, which are probably common to all types of acute circulatory failure regardless of the method of production. It is not maintained that all or the majority of instances of shock are due to the local loss of fluid from the blood stream. For example, the decline in blood pressure which may be associated with intra-abdominal operations, the perforation of hollow organs and injury to the brain are probably brought about by different mechanisms. Many different agencies may enter into the production of shock that is associated with operations. Among the factors that may result in a diminution in the circulating volume of blood may be included hemorrhage, sweating, the anesthetic, loss of plasma from the exposed surfaces, the pooling of blood in vessels that are dilated as a result of mechanical irritation or nervous reflexes, infection and the disease for which the operation is performed. The shock that develops following the perforation of a hollow organ appears, because of its sudden onset, to be mainly reflex in origin.

In conclusion, the term shock should be used in a general sense to designate a clinical syndrome that is familiar to all. The pallor, apathy, sweating, cold skin, vomiting and weak pulse form part of the fully developed picture. The work of recent years has shown that it is dependent on an inadequate supply of blood to the tissues, which may be brought about by the most diverse causes. Only the mechanism by which shock results following trauma to muscles and hemorrhage has been discussed in detail in this paper.

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DISCUSSION (*Abstract*)

Dr. J. Shelton Horsley, Richmond, Va.—Dr. Blalock has done interesting and constructive work in interpreting the phenomena of shock. First of all, he very properly classifies traumatic shock as differing from the so-called reflex shock, or nervous shock, that quickly follows trauma in certain portions of the body, such as the perforation of a duodenal ulcer or injury to the testicle. The type of traumatic shock that he describes has been considered by many, following the work of some eminent physiologists during the War, as due to histamine-like products that were supposed to be formed in the injured tissues, particularly in injured muscle. These products have never been isolated, and Dr. Blalock and his associates have been unable to demonstrate them.

I have had the pleasure of seeing some of Dr. Blalock's work in his laboratory: the care with which he estimates the loss of fluids from injured tissue and the large amount of plasma that exudes in the tissue after injury.

While there is some hemorrhage following the pulpefying injuries that produce traumatic shock, the loss of the corpuscular element of the blood is comparatively small, though much plasma escapes. This explains the high concentration of red blood cells in shock where the fluid elements of the plasma have escaped, whereas in hemorrhage both the corpuscular and fluid elements escape in equal proportion. However, slow hemorrhage may produce somewhat the same phenomenon.

A particularly interesting point brought out by Dr. Blalock is the hopelessness of treating late stages of shock. The terminal stages occur after the continued low pressure has produced such changes in the sensitive centers of the brain that even though the blood pressure is temporarily raised and the lost blood itself is fully replaced, recovery does not ensue. The experiments in which he has produced a low blood pressure by slow hemorrhage in dogs and maintained it at a low level for some time, and the dog has died even though by transfusion more blood was restored to him than was actually lost, are extremely impressive. I have in clinical expérience seen just this happen, when shock that was induced by postoperative hemorrhage was combated by transfusion. The shock was due to hemorrhage and had been treated by other means than transfusion until it was obvious that a transfusion was necessary. Though apparently much more blood was transfused than the patient had lost, the patient died of shock. The importance of not permitting the blood pressure to remain low for any great length of time should be emphasized.

It is for this reason that we have for several years insisted upon the intravenous administration of dex-

trose in Ringer's solution in every operation in which there is a likelihood of shock or bleeding. This administration is continued throughout the operation, and if it does not satisfactorily maintain the blood pressure a transfusion is given later.

By keeping the blood pressure above the shock level, which of course is variable for each individual depending upon his normal blood pressure, the avoidance of shock can usually be accomplished; but, if shock does occur, a prompt transfusion of blood and then a continuation of the dextrose in Ringer's solution will doubtless control it.

Dr. Wm. T. Rienhoff, Jr., Baltimore, Md.—Dr. Blalock's many contributions in the last few years to the study of secondary shock are well known. There are two points which I think should be emphasized.

One is, that in the animals in which the blood pressure was kept at a low level over certain periods of time and from which small amounts of blood were removed from time to time, there was produced a condition similar to secondary shock, although it was in reality also one of removal of blood: in other words, similar to hemorrhage. Dr. Blalock has shown that in these animals the usual response to blood transfusions demonstrated in secondary hemorrhage was not forthcoming, and that therefore to differentiate shock and hemorrhage on a basis of response to transfusions or the presence of concentration of red blood cells or the presence of petechial hemorrhage throughout the viscera is inaccurate. In the presence of a sustained low blood pressure the two conditions are so interwoven that it is almost impossible to differentiate them.

The association of a prolonged lowering of the blood pressure, coupled with the continued loss of blood over this period of time, has been shown experimentally by Dr. Blalock to be productive of petechial hemorrhages in the viscera, areas of necrosis in the liver, suprarenal and lung, together with hemorrhagic exudate into the intestinal canal. This brings to mind a possible explanation of the untoward effects of prolonged operations under anesthetics that are depressing to the blood pressure. For instance, it is well known that tribrommethyl alcohol (avertin) and spinal anesthesia cause lowering of the blood pressure in the beginning which lasts throughout an operation, and by some this has been regarded as being perfectly harmless. The continued loss of blood and shifting in the fluid balance of the tissues, which occurs during any operation due to drying of the tissues from exposure and bleeding, even though it be the minimum amount, might very well produce the same type of lesions in patients that Dr. Blalock has produced in animals, and again may explain some of the complications which have been encountered after the use of this type of anesthesia. I think this observation may very definitely serve, in part at least, to explain some of the unfortunate instances of vasomotor collapse, postoperative pneumonia, postoperative necrosis of the liver, and sudden deaths which have occurred following the use of these depressing anesthetics.

Dr. Blalock's work shows very definitely that the removal of blood to the point of producing a marked secondary anemia will not produce these lesions in the viscera unless this loss of blood is superimposed in an animal in which the blood pressure has been lowered to a level of seventy or so millimeters of mercury. If, as he said, there is a hemorrhagic exudate in the mucosa of the intestine there might very well be a hemorrhagic exudate in the capillaries of the lungs. There might also be petechial hemorrhages in the medulla which would also create a vasomotor collapse. The deaths that have occurred in our experience following the use of avertin have been of this type, namely: complete vasomotor collapse that has come on in the relatively early hours following operation.

Dr. Blalock's demonstration that the loss of fluid blood plasma in the traumatized extremity is equal to one-half the total blood volume is, I think, a contribution worthy of note. This point explains very well the clinical manifestations of a chronic condition that was formerly supposed to be due to the toxicity of a histamine-like substance.

SOME THERAPEUTIC PROCEDURES BASED UPON RECENT ADVANCES IN BIOLOGICAL CHEMISTRY*

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During recent years there has been a growing appreciation of the fact that in a wide variety of common clinical conditions alterations occur in the chemical equilibrium of the body which may in themselves be of such nature as to influence profoundly the clinical picture. Failure to recognize the existence of these changes and to adopt methods for restoration of normal chemical equilibrium may seriously handicap or vitiate completely the entire therapeutic program. The chemical changes occurring in the body in such conditions as diabetes and nephritis have been very thoroughly studied for many years and are fairly well understood. There are many other conditions, however, in which the chemical changes are of equal importance, but have not been so generally recognized.

It is the purpose of this paper to point out the significance of certain facts concerning the chemical composition of the body in health and in disease and to indicate the ways in which such information may be of practical value in the therapy of certain common clinical conditions. Some of the investigations to be discussed were carried out in our clinic and the observations were made on children, but the facts established are equally applicable to adults.

Technical difficulties generally preclude the possibility of determining the chemistry of body cells and tissue, but changes in the fixed tissues

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*Read in General Clinical Session, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

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of the body are to a very considerable extent reflected in the chemical composition of the blood.

Let us consider first certain conditions associated with variations in the water content of the blood. The amount of water in the blood is maintained at a constant level during health by a balance between absorption and excretion. Any increase in the water content of the blood, by dilution of the other components, results in a lowering of osmotic pressure; and a decrease in the water content results in a raising of osmotic pressure. The osmotic pressure tends to be maintained at all costs, solids or fluids being excreted or retained to accomplish this purpose, even though this may result in a disturbance of acid-base equilibrium, with the production of either acidosis or alkalosis, or in such a phenomenon as general edema.

A decrease in the water content of the blood, or anhydremia, may occur as a result of a disproportion between water intake and output. A decreased intake may be the result of fluid restriction or vomiting, and an increased output may be the result of severe diarrhea, pathological diuresis or excessive evaporation of water from the skin and lungs in the presence of high external temperatures. Anhydremia brought about in any of these ways leads to the excretion or destruction of certain constituents of the blood to a sufficient degree to restore normal osmotic pressure. This, however, necessarily leads to a decrease in blood volume, which in turn is followed by a constriction of peripheral blood vessels and a decreased volume flow of the blood, which may seriously impair the functional activities of the body.

The clinical evidences of anhydremia are loss of weight greater than can be accounted for by any other cause, a dry and slaty-grey colored skin, and a decreased secretion of urine of high specific gravity and containing albumin and numerous casts, even in the absence of pre-existing renal disease. Fever, unexplained on the basis of infection, is also a frequent manifestation.

The chemical changes occurring in the blood in anhydremia depend upon the nature of the underlying cause of the water deficiency. Where there has been simple deprivation of fluid, or excessive loss by evaporation, the blood is concentrated, has a high specific gravity and corpuscular count, and an increased concentration of serum proteins. Fluids and dissolved salts tend to pass from the tissues into the blood, leading to a shrinkage and desiccation of the tissues. Because of decreased urinary secretion, urea and other nonprotein nitrogen constituents may be retained in the blood. Retention of acid metabolites and the failure of neutralization of acids by ammonia formed in the relatively inactive kidney results in some degree of acidosis. The bicarbonate of the blood plasma is reduced in amount and in part replaced by sodium chloride and salts of organic acids.

When anhydremia occurs as the result of diarrhea, there occurs not only loss of fluid from the body, but also a loss of alkali by way of the bowel, which represents partially unabsorbed intestinal secretions. This often results in a significant depletion of blood bicarbonate. The blood chloride content, on the other hand, is usually considerably elevated and compensates, so far as osmotic pressure is concerned, for the depleted bicarbonate. When anhydremia occurs as the result of vomiting, especially if the vomiting be due to pyloric or high intestinal obstruction, there occurs a loss not only of fluid but of hydrochloric acid and chlorides of the gastric juice. This leads to changes in the blood which are the reverse of those occurring as the result of diarrhea. The blood chlorides are decreased and there is a corresponding increase in bicarbonate. This constitutes the condition of alkalosis, the antithesis of acidosis, but none the less serious. When both vomiting and diarrhea occur, both bicarbonate and chlorides are lost. The one may compensate for the other, but acidosis is more likely to be the predominating feature.

When anhydremia results from diarrhea and acidosis has occurred, the respirations will be deep and pauseless. If, on the other hand, acid has been lost through vomiting and alkalosis has occurred, the respirations will become slow, irregular and shallow, and the patient may show the characteristic manifestations of tetany, that is to say, corpopedal spasm, Trousseau's sign, a positive facial phenomenon (Chvostek's sign) or even convulsions. But little information can be gained by examination of the urine, for even in the presence of severe alkalosis, the urine may be strongly acid, due to the fact that alkali is retained and not excreted.

In the treatment of anhydremia, water is of course indicated in any event, but what else is to be given in addition will depend upon the nature of the underlying cause and upon the chemical changes induced. Water administration alone, by restoring a normal blood volume and circulation, leads to the re-establishment of renal secretion and may bring about a return to normal conditions. When acidosis is extreme,

however, recovery is hastened by the administration of alkali, whereas in the presence of alkalosis with high blood bicarbonate and low chloride the administration of chlorides is indicated. There is a potential danger in the administration of fluids containing too high a concentration of chlorides to patients with acidosis, and likewise a danger in the administration of alkali to those with alkalosis. It is not always possible to administer water alone. Vomiting and diarrhea may preclude the giving of any considerable amounts of fluid by mouth or by rectum, so that parenteral methods of administration must be adopted.

When fluid is administered subcutaneously, intravenously or intraperitoneally, water alone cannot be used; a solution must be made more nearly isotonic with the blood and tissues. In those cases in which the indications are not clear cut for the use of either chlorides or alkali, a dextrose (d-glucose) solution is usually a fairly satisfactory form in which to administer parenteral fluid, except of course in the case of diabetes. Dextrose is consumed, leaving behind only water. A further advantage is that the solution of dextrose also supplies food, which may be sorely needed. Dextrose in 10 per cent solution may safely be administered intravenously at a rate of 3 or 4 c. c. per kilogram of body weight per hour, which is equivalent to from 3 to 5 c. c. per minute in the case of an adult of average size. Injection at this rate does not result in glycosuria or untoward symptoms. The solution may be run in continuously over long periods of time. This procedure of continuous dextrose injection, known as "venoclysis," was first strongly advocated by Dr. George A. Hendon,[1] of Louisville, Kentucky. It is a life-saving measure.

In those cases in which acidosis is known to exist, a fluid containing alkali, or potential alkali, should be administered. There are serious technical difficulties in preparing suitable solutions of sodium bicarbonate for parenteral use. The use of sodium lactate obviates these difficulties. This salt is neutral in reaction and when isotonic, the solution is not irritating to the tissues. It may be given intravenously, subcutaneously or intraperitoneally with safety. Sodium lactate is converted into bicarbonate in the body at a sufficiently rapid rate to supply alkali as needed and yet not so rapidly as to produce an uncompensated alkalosis when given in suitable dosage. Dr. Alexis F. Hartmann,[2] of Washington University, has placed this form of alkali therapy on a sound scientific basis and has determined the effective dose and manner of administration.

A one-sixth molar solution of sodium lactate is isotonic. The maximum dose injected at one time should usually not exceed 60 c. c. per kilogram of body weight. When this amount is injected slowly over a half hour period, the blood carbon dioxide may be expected to rise approximately 25 to 35 volumes per cent during the following hour. If one knows the blood carbon dioxide content in advance, it is possible to calculate with a high degree of accuracy the amount of lactate required to restore normal conditions. The lactate solution is readily prepared for use by the dilution of molar sodium lactate, now available in ampoules.* Sodium lactate is useful not only for the treatment of acidosis resulting from anhydremia, but equally useful in the acidosis of diabetes and other forms of ketosis.

In the treatment of the acidosis of anhydremia, either dextrose solution or sodium lactate is preferable to normal saline. An isotonic solution of sodium chloride (0.9 per cent) has a higher chloride concentration than the blood, hence when the chlorides of the blood are already above normal, the injection of a still higher concentration of chloride may result in a further replacement of bicarbonate by chlorides, and an increase in the acidosis, especially if, as is often the case, urinary secretion is minimal. Ringer's solution is somewhat preferable to simple sodium chloride because of the other salts present. Better still is a solution composed of a mixture of Ringer's solution and isotonic sodium lactate (Hartmann's solution).[3]† Such a combined solution contains less chloride than blood, hence does not increase acidosis. It supplies sufficient chloride, however, to restore moderate depletion occurring as the result of vomiting. In those instances in which it is not possible to make blood chemical analyses, such a combined solution will serve to correct either acidosis or alkalosis without the danger of increasing either.

In well marked cases of uncomplicated alkalosis due to vomiting, sodium chloride solution alone may be used to advantage.

Let us now turn to a consideration of another important constituent of the blood, the sugar. A large proportion of the total food absorbed is converted into dextrose and carried by way of the blood to the tissues, there to be metabolized; but the dextrose of the blood represents

*The Eli Lilly Company, Indianapolis, Indiana.

†Now available in ampoule form. Eli Lilly Company, Indianapolis, Indiana.

more than just food material in transit. Dextrose is an essential constituent of the blood and exerts a definite physiological action. The amount of dextrose present in the blood of normal individuals in the postabsorptive state averages about 100 mg. per 100 c. c. of blood, or 80 mg. "true" sugar. The amount increases by from 20 to 40 mg. shortly after the ingestion of a meal containing carbohydrate, but rarely rises above 150 mg. in normal individuals. In the diabetic, the concentration may increase to as high as 500 or 1,000 mg. per 100 c. c., and under such conditions dextrose appears in the urine. An increase in blood sugar in itself does not lead to any very serious symptoms, however, and causes no especially harmful changes in the body. A low blood sugar concentration, on the other hand, does lead to definite and at times serious symptoms. A fall in blood sugar to 60 or 70 mg. is usually associated with hunger contractions of the stomach, weakness, an "all gone" feeling, mental and physical lethargy and at times trembling and profuse perspiration. With a still greater fall in blood sugar there may be a subnormal temperature, a sensation of numbness, mental confusion and incoherent speech. The individual may behave very much like one suffering from alcoholic intoxication. Generalized convulsions, followed by coma, may occur when the blood sugar drops to very low levels, generally below 40 or 50 mg. In these latter cases, the clinical picture may closely simulate epilepsy. Such hypoglycemic reactions are observed after overdosage with insulin, but also occur in individuals who have not been given insulin. The symptoms are all promptly relieved by the administration of sugar by mouth, or by dextrose intravenously.

A moderate degree of hypoglycemia is frequently observed. It occurs after overexertion. Certain individuals are especially prone to the development of hypoglycemia unless they partake of food at fairly frequent intervals, and it is possible that this may be due to a superabundant secretion of insulin. In 1924, Seale Harris,[4] of Birmingham, Alabama, reported on a group of patients who had abnormally low blood sugar values, and who presented some of the symptoms just enumerated. He suggested that these patients were suffering from an overproduction of insulin.

A tendency to hypoglycemia is especially common in infants and young children. In infancy the symptoms are irritability, colic and continuous crying; in older children, emotional excitement, undue sensitiveness, fatiguability and often periodic attacks of vomiting. Occasionally one observes more serious manifestations. Reports have come from a number of clinics in recent years of attacks of epileptiform convulsions, directly attributable to hypoglycemia. We have observed seven such cases in recent years. Our suspicions as to the nature of the convulsions were in each case aroused because of the occurrence of convulsions in the early morning hours when there had been the longest time of abstention from food. In each of our cases the blood sugar was below 40 mg. at the time the convulsions occurred. The symptoms were in all instances promptly relieved by the intravenous administration of dextrose. In several of these children, regulation of the diet with a liberal intake of carbohydrate resulted in a cessation of the attacks. Carbohydrate feeding at midnight was found to be of especial value. It was found, however, that infection of any type associated with lack of appetite and decreased food intake tended to cause a reappearance of the symptoms.

In one instance, a year old infant had repeated attacks of convulsions, which at times involved only a portion of the body. The child's mental development was retarded. The blood sugar was consistently below normal limits, usually between 30 and 40 mg., and preceding the convulsions it fell to as low as 19 mg. Dietetic treatment was in this case entirely unavailing. A pancreatic tumor was suspected and an exploratory operation was performed, but no tumor was found. Since this child evidently had an oversecretion of insulin, Dr. Evarts A. Graham, at the time of operation, removed approximately seven-eighths of the pancreas, with the idea of reducing the amount of insulin secreted. Following this operation the blood sugar rose to 500 mg. and sugar appeared in the urine. At the end of a week, however, the blood sugar was within normal limits and remained so. There was a prompt cessation of the convulsive attacks.

In other patients showing the symptoms described, definite tumors have been found, consisting largely of Langerhans island cells and containing enormous amounts of insulin. The first of these cases was reported by Wilder and his colleagues at the Mayo Clinic.[5]

The patient, a physician, was subject to sudden attacks of weakness, faintness, paresthesia, accompanied by profuse perspiration and trembling. For a time the attacks were prevented by eating frequently. Later the attacks became more severe and coma and death followed. At autopsy a tumor composed of islet tissue was found in the pancreas. A similar case was reported in 1928 by Thalhimer and Murphy.[6] In 1929, Campbell[7] and his colleagues at the Toronto General Hospital reported on a patient who complained of attacks of severe exhaustion accompanied by sweating,

vomiting and violent convulsions, followed by coma. At times the patient appeared as if drunk. The blood sugar was low and the attacks were controlled temporarily by the administration of carbohydrate. At operation a tumor of the pancreas was removed, which consisted of islet tissue and from which insulin was recovered. Following the removal of this tumor, the blood sugar reached a normal level and there was complete disappearance of the subjective and objective symptoms. Altogether, seven such cases have now been reported, three of which were operated upon by Graham[8] and his colleagues from the Surgical Department of Washington University. In the case of one of these patients, a pancreatic tumor was removed, without cessation of symptoms. Subsequently the tumor was found to contain neither island tissue nor insulin. At a second operation another small tumor was found in the pancreas, which was removed, and this was followed by disappearance of hypoglycemic symptoms and a return of blood sugar to normal, or slightly high values.

The combination of symptoms resembling alcoholic intoxication, associated with epileptiform convulsions, relieved by the taking of food, should always suggest the possibility either of an islet tumor of the pancreas or hyperactivity of existing islets of Langerhans. The finding of a low blood sugar is strong confirmatory evidence. In such instances operative procedures should seriously be considered.

Although an excess production of insulin in the body may, by producing hypoglycemia, lead to untoward symptoms, there are times when insulin injections may to advantage be used in non-diabetic individuals with the purpose of deliberately bringing about hypoglycemia, hunger contractions of the stomach and an increased appetite. It has been a matter of common observation that diabetic patients, especially children, treated with insulin often become excessively fat. It has indeed been claimed by some that one of the chief causes of obesity is hyperinsulinism. These facts suggested to us the use of insulin in undernourished infants and children.[9]

One often sees infants who have become badly undernourished, who have poor appetites and in whom it is impossible to bring about a consistent gain in weight, even with well balanced feedings. In some instances repeated injections of fairly large amounts of dextrose solution are effective. We have found, however, that if the dextrose is combined with insulin, gain in weight is more prompt and greater. We have found the injection of a 20 per cent solution of dextrose with insulin added in an amount equivalent to one unit to each 2 or 3 gm. of dextrose to be an effective means of treatment. Almost equally effective is the mere administration of insulin before feedings. The amount of insulin we have given has been such as would theoretically lower the blood sugar one-half and this corresponds in the case of the average infant to from 2 to 3 units. The injection is given about 30 minutes before the feeding so that the maximum effect will be present at the time of the feeding. In the case of very badly undernourished infants who have been taking but little food, insulin should be given cautiously at the start in order to avoid the possibility of marked hypoglycemic reactions. The injection of insulin has in our experience usually resulted in considerable increase in appetite and in food intake with coincident gain in weight. This method of treatment has been in use in our clinic for the past ten years. It has been applied by others not only to infants, but to older children, and to adults with marked success, and we have come to look upon this procedure as a standby when other means have been exhausted, in those cases in which the undernutrition is not dependent upon recognizable disease.

We have discussed some of the phenomena which are associated with changes in the chemical equilibrium of the blood. Only a few have been touched upon, but when one appreciates the nature of the chemical disturbances which are likely to result in the course of clinical conditions, he is in a position to apply rational therapy. In clinical medicine, it often pays to be chemically minded.

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HYPOGLYCEMIA DUE TO ADENOMA OF THE ISLETS OF LANGERHANS*

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The subject of carbohydrate metabolism is at the present time confused and poorly understood. Several organs and tissues are involved. Apparently it is extremely important to the normal functioning of the body that the blood sugar level be kept within certain well-defined limits and it is common knowledge that the organ apparently involved more than any other is the islets of Langerhans of the pancreas. This is true in spite of the fact that in many cases of diabetes mellitus no lesions of any significance are found in the pancreas. The isolation of insulin has influenced us in this belief perhaps more than any other factor.

Shortly after the appearance of insulin it became apparent that the lowering of the normal level of blood sugar was often associated with rather dramatic symptoms. These symptoms were grouped under the general heading of insulin shock and were often quite varied in type, consisting in the milder cases of hunger, restlessness, pallor, sweating, tremor and the like. When the sugar was markedly lowered, automatic movements suggesting a *petit mal* epileptic attack occurred or in severer cases stupor, coma and convulsions. It must be constantly borne in mind that these symptoms are not due to insulin itself, but to hypoglycemia, and they may be produced by any agent that can lower the blood sugar level. These agents are numerous. We shall not consider them in detail here, for they involve the whole subject of carbohydrate metabolism. We shall, instead, confine ourselves to spontaneous hypoglycemia definitely pancreated in origin and specifically associated with tumors composed of islet cells.

That a clinical syndrome caused by spontaneous hypoglycemia can be due to the pancreas was first pointed out by Harris[1] in 1924, when he reported several cases and gave us the terms "hyperinsulinism" and "dysinsulinism." The first anatomical proof of this conception appeared in 1927, when Allen[2] reported a patient with carcinoma of the islets of Langerhans dying with hypoglycemic symptoms. This was followed in 1929 by the successful removal of a localized tumor of the islets with relief of symptoms by Howland,[3] Campbell, Maltby and Robinson. Since then a rather extensive literature on the subject has developed which we shall not try to review here, as it has been given elsewhere by ourselves and others.

At the Barnes Hospital there have been five patients with hypoglycemic symptoms who have been operated upon and from whom an adenoma composed of islet cell tissue has been successfully removed. The hypoglycemia disappeared immediately after the operation and up to the present time the clinical course of these patients has been satisfactory. There have likewise been three tumors of this type found at autopsy, one associated with hypoglycemia, one with no apparent disturbance in carbohydrate metabolism and one with a mild diabetes. Detailed reports of some of these cases have already been made.[4] Others are in press.[5] In the present report we should like to emphasize certain features about this type of lesion.

Most of these patients presented a history of gradual onset with symptoms varying from hunger, weakness, dizziness and a feeling of apprehension to that of momentary loss of consciousness with associated automatic movements lasting from a few seconds to several minutes. These symptoms all followed a long starvation period at first, and were especially common just before breakfast. They were likewise often seen when severe muscular exercise directly preceded a meal. They usually disappeared or could be aborted by the ingestion of food. There was a tendency for the attacks to become more frequent and at the same time more severe until by the time we saw the patient in most instances convulsive attacks associated with coma were common. Another finding which had become marked in at least two of our patients was a definite mental deterioration. A striking feature in the typical history is that the patient usually sooner or later notices the association between the attacks and hunger. In fact, most of them have found that the eating of food with a high carbohydrate content is most effective. They likewise volunteer the information that most sedative drugs have been found to be of little value.

We cannot stress the importance of such a history too strongly. At the same time we realize that there are exceptions. One of our patients first noticed rather typical *grand mal* convulsions at the onset which were not no-

*Read in Section on Surgery, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

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ticeably relieved by food, but were aided considerably by the taking of beverages containing caffeine. We have likewise seen patients with a rather characteristic history who presented a normal carbohydrate metabolism so far as we could determine.

Physical examination has been unusually barren in so far as positive findings are concerned. One exception is the rather frequent occurrence of a unilateral or bilateral Babinski sign. We have seen this often enough, as have others, to attach considerable importance to it. Slurring, tremulous speech has also been occasionally noted. Other neurological changes have been inconstant.

Routine laboratory studies have all been within normal limits with the exception of the blood chemistry. The most important single finding is that of hypoglycemia. Without it, the clinical picture is not complete. With it, the clinical history can receive its proper interpretation. This condition offers a striking example of the importance of the knowledge of the fundamentals of physiology and chemistry on the part of the general surgeon. Where so much depends upon a laboratory test he must be confident of the interpretation and the accuracy of that test.

After the presence of hypoglycemia is confirmed it is often difficult to determine whether or not it is of pancreatic origin. The infrequent occurrence of pituitary and liver lesions with such findings must be considered. It is conceivable that when the hypoglycemia is the result of pituitary insufficiency no other evidence of pituitary disease may be found. For all practical purposes, however, it is usually possible to demonstrate a destruction of the sella turcica roentgenologically and the presence of visual field changes. Likewise the hypoglycemia is generally not marked, though this is not always the case.[6] Hepatic insufficiency in rare instances may evidence itself as a hypoglycemia. This has been noticed in tumors of the liver and in toxic hepatitis where the liver either contains no glycogen or is unable to store glycogen. At such a time it is possible for a normal insulin secretion to cause a hypoglycemic reaction. Where the injection of epinephrine raises the blood sugar and relieves the patient of his symptoms temporarily it is generally safe to assume that one is not dealing with hepatic insufficiency. Yet when epinephrine fails to raise the blood sugar it does not necessarily follow that the primary disease is hepatic in origin. We have observed two patients in whom hypoglycemia from an islet adenoma was so severe that such a rise did not occur. Hypoglycemia from other cause usually offers but little diagnostic difficulty. This has been discussed in detail in a recent monograph on the subject by Sigwald.[7]

Children not infrequently present an unstable carbohydrate mechanism. At times they present a clinical history almost identical with that seen in an islet cell tumor. The hypoglycemia, however, is usually temporary. It may occur from the sudden withdrawal of sugars after a prolonged high carbohydrate diet. Strangely enough it may appear during infections when exactly the opposite situation would be expected. Gray and Feemster[8] reported an autopsy on an infant whose mother was a diabetic. They noticed a marked hypertrophy of the islets of Langerhans. Recently at the St. Louis Children's Hospital another such patient was seen. The child developed hypoglycemic convulsions shortly after birth, which were relieved with sugar. The mother was a moderately severe diabetic. After several days, by gradually reducing the amount of sugar in the diet of the infant, the blood sugar became normal and remained so. This condition is of interest in view of the fact that the placenta is apparently impermeable to insulin. It is perhaps best explained on the basis of a high maternal blood sugar reaching the fetal pancreas and causing increased insulin output in the fetal circulation. We know of no reports of active islet cell tumors in the pancreas of infants.

The diagnosis of this clinical entity thus rests upon the establishment of a well defined group of symptoms in an adult, associated with a more or less constant low blood sugar level in the fasting specimen. There must also be demonstrated a high carbohydrate tolerance when glucose is given by mouth and blood sugar estimations are made. This high tolerance curve in our experience varies to some extent with the severity of the disease. However, it is constantly present.

The adenoma is usually situated in the tail or body of the pancreas. In most cases it has been 1 to 2 cm. in diameter and clearly demarcated from the rest of the pancreas by virtue of its reddish color. It may at times resemble a small hematoma within the pancreatic tissue. Ordinarily the tumor is not especially hard and if located within the substance of the body or head of the pancreas it may easily be overlooked.

It will be recalled that the islets of Langerhans, like the acini, are formed originally from

pancreatic duct epithelium. The normal islet is composed of several types of cells, distinguished chiefly by the staining qualities of the cytoplasmic granules present. They probably vary somewhat in function. The cell type we are most interested in is the so-called *beta* cell, which can be distinguished in the Zenker fixed tissue by the Mallory-azan stain. The cytoplasmic granules are small and, in the latter stain, of a lilac color. These granules probably represent an intracellular antecedent of insulin. The cells are arranged closely around capillaries and with a special technic have been observed to form secretory vacuoles which were ejected directly into the capillary.[9]

Since these cells rise originally from ducts, in tumors one may expect all types of differentiation varying from the more or less embryonic duct cell to the more mature *beta* cell. Likewise, if this conception is correct, the more mature the cell is when considering the tumor as a whole, the more severe the clinical hypoglycemia will be. A more detailed analysis of the cytology of these tumors which is being reported elsewhere[10] seems to substantiate this idea. It may be possible that an immature cell may secrete an immature type of insulin. If so this would tend to agree with the "dysinsulinism" theory first brought out by Harris. Unfortunately, at the present time our knowledge of the chemistry of insulin is so vague that this question must for the time being remain unsettled.

Degenerative phenomena are common in these tumors. The most frequent is that ot hyalinization which at times may be extreme. We have observed in one case complete replacement of the islet tissue by this collagen-like substance which apparently has its origin beneath the endothelium of the capillaries. Hemorrhages are likewise common and in two tumors we have seen areas of calcification.

Islet adenomata are usually single. They may be multiple. We have reported one such case and there are two others in the literature.[11 12] It is important to bear this in mind, and even if a tumor is found at operation, the entire pancreas should be carefully explored.

The question of malignancy has offered considerable difficulty, as encapsulation of the growth is not always perfect and the morphology is often confusing. The situation is not unlike that seen in the thyroid gland. Regardless of the cellular structure, generally we feel that if the capsule of the pancreas has not been invaded, if there are no metastases and no invasion of the blood vessels, it is wise to consider the lesion benign. However, we have followed some of these patients for an insufficient time to dogmatize on this point.

Clinical surgery offers few examples where the recovery is so complete or so dramatic as from the complete removal of an islet tumor. So unanimous has been this opinion that it would seem unnecessary to stress it here were it not for the fact that there is a tendency on the part of some internists to treat these patients with diet alone. We feel that while it is wise to observe such a patient until the constancy of the hypoglycemia is established, there are certain dangers to be considered if this is carried on too long. Perhaps the most important of these is mental deterioration. While there is a tendency for this to improve after operation, the improvement is slow and may not be complete. The tendency for a tumor to undergo malignant change must likewise be considered as must the effect of a lowered blood sugar on cardiac muscle.

The surgical technic needs little description. Probably the most satisfactory approach is through a left rectus incision exposing the pancreas through the gastrocolic or gastrohepatic omentum, depending upon the habitus of the patient. We repeat that it is necessary to mobilize the pancreas so that it can be rotated and the posterior surface examined as far forward as the head. A drain should always be placed near the pancreatic stump, as small ducts are usually severed. Those pancreatic fistulae that have developed have all closed spontaneously after a few weeks and have never given much trouble. In one case secondary hemorrhage occurred, which, however, was not serious.

So far we have said little about those reported cases in which a typical hypoglycemia existed and no tumor was found. The procedure advocated by the Finneys,[13] who reported the first lesion of this type, of removal of a portion of the pancreas sounds reasonable. This has since been done by others.[14 15 16] It must be remembered that approximately nine-tenths of the pancreas can be removed experimentally before producing glycosuria. It is probably necessary, therefore, to remove a large portion of the pancreas to have any definite effect on the blood sugar.

In cases of this type in which surgery has been unsuccessful it may be possible to affect the hypoglycemia by gradually lowering the sugar intake of the patient and increasing the fat. It is a well known fact that the secretion of insulin is increased by the feeding of sugar,

and while sugar is necessary in an acute attack, it is probably advisable to reduce it gradually in the quiescent stage. The carbohydrate requirement in one of our patients rose from 300 to 900 grams a day after he was fed for several days on glucose alone. This was brought back down to 300 grams after about two weeks, during which time the carbohydrate in his diet was decreased and the fat increased.

Because of the tendency to hyperglycemia in toxic thyroid disease, thyroid extract has occasionally been advocated. As it is probable that this action is not due to an insulin antagonism, but rather to increased glycogenolysis, such therapy is of little value and at times may conceivably be dangerous. This likewise applies to the use of epinephrine.

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DISCUSSION (*Abstract*)

Dr. J. M. T. Finney, Baltimore, Md.—The subject of hypoglycemia of hyperinsulin was first brought to the attention of the profession by a member of this Association, Dr. Seale Harris, in 1924, when he reported several cases.

Dr. Womack has summarized in his paper about all that is known concerning the condition at the present time.

Surgery of the pancreas is a comparatively recent development. There are those here, I am sure, who will recall the fact that Mikulicz's over-emphasis, perhaps, upon the danger of operation upon the pancreas so influenced the profession as to delay for many years the development of the surgery of this organ. We now know, of course, that within certain limits operation on the pancreas for a variety of conditions is a feasible and comparatively safe procedure. Personally, my experience with resection of the pancreas for a variety of conditions led me, in company with my son, J. M. T. Finney, Jr., to advocate the removal of a portion of the pancreas in order to reduce the number of the islands of Langerhans. While in our case only partial relief was secured, the idea is theoretically sound. Of course, where adenomata of the islets are present, their removal is indicated.

Dr. Seale Harris, Birmingham, Ala.—We owe a great deal to the surgeons for our present knowledge of many diseases. We did not know much about thyroid diseases until the surgeons became interested in the subject, and we knew but little concerning pituitary disorders until the surgeons found that the hypophysis could be attacked surgically; and now that the surgeons have learned that patients may be cured of another serious malady, hyperinsulinism, by pancreatic operations, we are learning much from them about a disease entity of another endocrine organ. Cushing said of adenomas of the hypophysis: "They are veritable stills of secretion." Likewise the adenomas of the pancreas seem to be unregulated "stills" of insulin secretion, the manifestations of which are those of the severe reactions from an overdose of insulin.

My unimportant observation in 1924, when I reported five cases of hyperinsulinism, the antithesis of diabetes mellitus (hypoinsulinism) passed almost unnoticed until 1927, when W. J. Mayo operated upon a patient with an islet cell carcinoma which Wilder and his associates proved secreted insulin. This was the first case of proved hyperinsulinism. Shortly afterwards Dr. Finney did the first resection of the pancreas for hyperinsulinism; and a few months later Howland, Campbell and their associates made a preoperative diagnosis of a tumor of the islet cells, and by removal of the carcinoma cured a patient who had had epileptiform convulsions for a number of years. Later the problem was attacked by Washington University surgeons who have operated upon and have cured five patients who had recurring attacks of convulsions and unconsciousness, and who were doomed without surgery.

Recently in the Army Medical Library in Washington I reviewed the literature on hyperinsulinism, including the type due to insulomas. A number of cases of hyperinsulinism have been reported in England.

Cammidge in London has reported 200 cases of "chronic hypoglycemia," but no case of islet cell adenoma had been operated upon in England. Sippe and Bostick in Brisbane, Australia, reported 25 cases, but no adenomas. In France, Germany, Norway, Sweden and Holland a number of cases of hyperinsulinism have been reported, but no European surgeon has operated upon a patient with adenoma of the islands of Langerhans. It is gratifying to know that American surgery, certainly in the field of the pancreas, leads the world.

Unquestionably, adenomas of the pancreas occur frequently, but until recently they have not been diagnosed; just as adenomas of the thyroid, and adenomas of the hypophysis, were not recognized and operated upon until very recent years. It is not an accident that five cases of adenomas have been recognized by the internists, and operated upon by the surgeons, connected with Washington University. They simply have been looking for such cases and have known how to diagnose them when they saw them.

Surgery of the pancreas is an established procedure in the treatment of the severe forms of hyperinsulinism, particularly the islet cell adenomas. In the cases in which there are pronounced hypoglycemic symptoms such as recurring attacks of unconsciousness, with and without convulsions, which have resisted dietary management, and adenomas are not found in exploratory laparotomies, resection of the pancreas seems likely to become an accepted surgical procedure, just as subtotal thyroidectomy without adenomas of the thyroid has relieved many cases of hyperthyroidism.

The positive diagnosis of adenomas of the pancreas is difficult and can rarely be made with certainty without an exploratory operation. The anamnesis is important. A history of recurring attacks of convulsions and unconsciousness, three or four hours after meals, during the night or before breakfast, certainly suggests hypoglycemia as the exciting factor. Abdominal pain has been a prominent symptom in a number of cases that have been reported. Some of these patients have had operations for appendicitis and for gallbladder diseases without relief of symptoms.

Blood sugar studies are necessary in order to prove that hypoglycemia is associated with the symptoms. Therefore a good laboratory is the *sine qua non* in the diagnosis of hyperinsulinism. The glucose tolerance test, which consists of a fasting blood sugar test, then giving one and a half grams of dextrose per kilo of body weight, to be followed by hourly blood sugar tests for six hours, usually reveals low blood sugars, particularly in the five- and six-hour readings. One fasting blood sugar, or one glucose tolerance test, is not always sufficient to make a positive diagnosis of hyperinsulinism. Cushing observed in hyperpituitarism that there are undulations, or waves, of accelerated hypophyseal secretions, and so there seem to be periods when the patient with hyperinsulinism will have normal blood sugar readings and at other times marked hypoglycemia. In making a glucose tolerance test it seems important for the patient not to lie down during the tests, but to take about the same amount of exercise that he does in carrying on his ordinary activities, because blood sugar readings are higher when the patient is at rest than when he is taking exercise.

SOME NEW DEVELOPMENTS IN RENAL SURGERY*

By Oswald Swinney Lowsley,
A.B., M.D., F.A.C.S.,
New York, N. Y.

The introduction of ribbon gut into surgery of the kidney has stimulated a great deal of new and interesting experimental work which is worthy of brief mention at this time.†

The material is an animal tissue. The suture material designed expressly for use in this experiment consists of flat ribbons of untwisted gut 45 to 65 cm. in length, 1.8 to 2.0 in width, and in thickness no more than that of fine rice paper. Packed in alcohol in the usual type of aseptic catgut tube, it remains thoroughly pliable, though it shows a tendency to dry rapidly when exposed to air, and when dry is no longer adequately pliable. It may, however, be readily softened again by moistening with physiological saline.

In the animal experiments it has been used in bands one-half the standard width, that is, approximately 0.8 cm., but in operations on human beings, the full width has been used. It has in all instances been tied in the same manner as are ordinary types of catgut. The width of the material has not interfered with adequate knots, and the tape itself has shown a tendency to twist over a distance of only about a centimeter immediately adjacent to the knot. In no instances have we noted any tendency to slip on the part of the knot. *In vitro* experiments, conducted by the manufacturers, have indicated that the tape is absorbable in 4 to 5 days. Up to this time, this has not been confirmed by our observations; the tape has been found entirely intact, though of lesser tensile strength, at the end of 23 days.

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*Read in General Clinical Session, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

*From the Department of Urology (James Buchanan Brady Foundation) of the New York Hospital.

†The experimental work and manufacture of this material was done in the laboratories of Davis & Geck, to whom the author is greatly indebted.

The author is also greatly indebted to Mr. Wm. P. Didusch for suggesting this problem to Dr. Ralph O. Clock, who developed the material, and to Dr. C. C. Bishop and Dr. R. D. Bullard, who helped with the preliminary experiments.

The animal experiments necessary in perfecting the methods proposed herein were conducted in the Department of Experimental Surgery at the New York Hospital. The author is particularly grateful to Professor George Heuer and Professor Joshua Sweet and his assistants for their hearty cooperation.

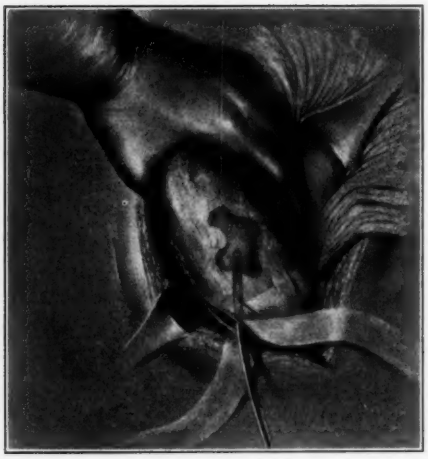

Fig. 1

Illustration shows a large stone being removed from the kidney pelvis through a nephrotomy wound in the lower pole, the ribbon gut already being in place.

The first work undertaken with this material consisted of the repair of renal wounds. We first used rabbit kidneys, which proved to be too small for practical use. Later a series of sixteen dogs were utilized.

Dog kidneys proved to be entirely satisfactory for experimental purposes. The animals were sacrificed at various periods after nephrotomy had been performed and the kidneys examined demonstrated several important facts.

The ribbon gut is fixed by means of straps made out of the fibrous capsule of the kidney. The material is held exactly in the position in which it is placed.* The material is so sterilized and packed that it can be kept indefinitely without spoiling and is therefore better than fascia lata or any of the materials that have been used heretofore.

It was discovered that the kidney wound could be closed efficiently by tying the ribbon around it, making it unnecessary to stick needles through the kidney substance. The advantage of avoiding the latter is tremendous because the scar produced by tying the kidney together is less than 5 per cent as large as the area of ischemia and ultimate scarification that is produced by placing a mattress suture through the kidney cortex, which causes a fan-shaped area of destruction extending through the cortex to the capsule.

*Unknown to the author Dr. O. S. Fowler, of Denver, Colorado, had used this method as early as 1913, using fascia lata for material.

The bleeding can be effectively controlled by using a thin layer of fat, buttered on the cut surface of the kidney.

Experiments* and clinical observation have proven beyond a doubt that fat is by far the

Fig. 2

The ribbon gut is placed with the knot tied away from the wound in the kidney. A small piece of fat is buttered upon the surface of the incision through the kidney cortex. A tube is placed in the pelvis and fixed in position by a catgut strand passed through the edge of the ribbon gut.

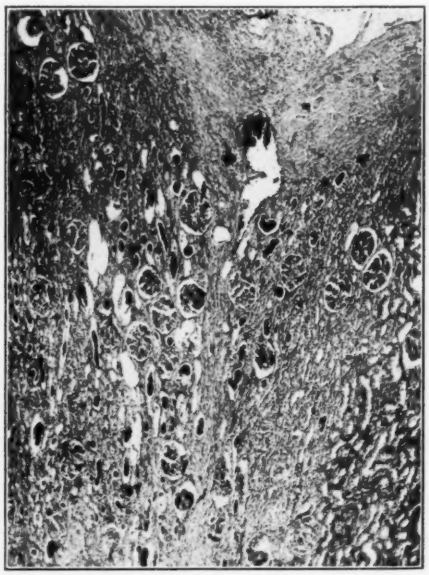

Fig. 3

The capsule over the incision is thickened. A narrow scar, part of which is shown in the center of the photomicrograph, extends from this to the pelvis. A narrow zone of partially atrophic renal cortex is seen on either side. Dog C O 38, Pathology No. 18324.

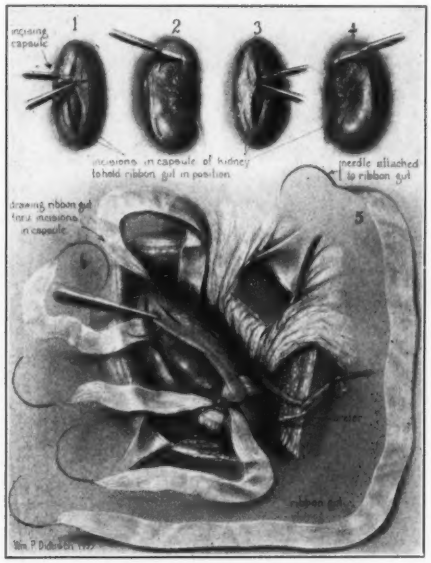

Fig. 4

(1) Capsule is incised and stripped back. Straps are made in edges of the fibrous capsule for the reception of the chromic ribbon gut. (2) (3) and (4) Additional straps are made in the fibrous capsule. (5) Chromic ribbon gut studded with a needle at each end. (6) Shows the placing of chromic ribbon gut through the prepared straps. It is tied without compressing the cortex or leaving the capsule open for the formation of adhesions to fix the kidney.

best agent for hemostasis in kidney wounds. Our own experimental work proves conclusively that fat will control hemorrhage in the kidney in one-tenth the time that bits of muscle will accomplish this end.

Fortunately, none of our human cases of nephrotomy have died, so our only method of determining the exact extent of the damage done in human cases has been by postoperative functional tests and postoperative pyelograms by the intravenous and retrograde methods. These have demonstrated beyond a shadow of doubt that the functional damage done is much less than that of the methods of repair formerly used.

The author has been dissatisfied with the operative method utilized in nephropexy. The older method in which needles were inserted through the kidney cortex was quite destructive and the newer excellent method proposed by Deming, of New Haven, has not always been successful in our hands in holding the kidney in place.

Therefore, ribbon gut was subjected to a chromacizing process. Needles were fixed at each end of the chromic ribbon gut for the purpose of facilitating its fixation. Experimentation shows that *in vitro* this material is absorbed only after 100 days. Later experience has proven that the first chromacized ribbon gut was too resistant to absorption, so material has been developed which is absorbed in three weeks.

Without taking part in any discussion whatever as to the circumstances under which one shall do a nephropexy, the author proposes a new operation for fixation of the kidney, once a decision is made that it is a suitable case for the procedure.

This operation was developed upon dogs and only after 12 animals had been used as experimental material was the operation attempted upon a human being.

TECHNIC

The kidney is exposed in the usual manner and dissected free from surrounding structures by separating adhesions and other clinging tissues. Two sets of straps, usually three or four in number, are then made in the fibrous capsule surrounding the upper and lower poles of the organ. The chromic ribbon gut, with a needle attached to each end, is then passed through the straps and tied with the knot on its anterior surface. It must be tied loosely, so as not to cause compression of the cortical substance, but tightly enough so that it will hold firmly.

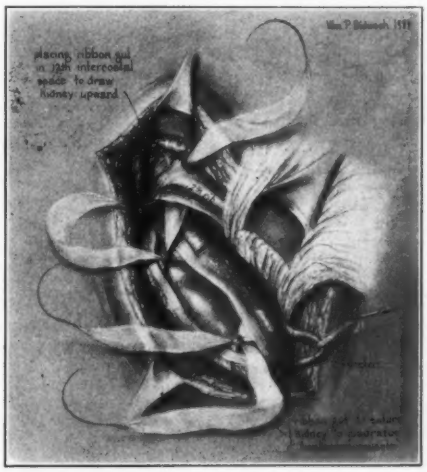

Fig. 5

The needles followed by the chromic ribbon gut are passed through the intercostal musculature about one inch apart.

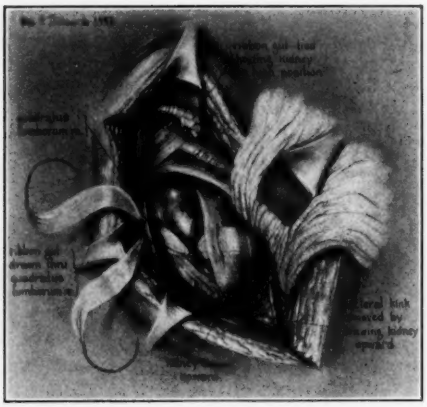

Fig. 6

The chromic ribbon gut around the upper pole is tied above. The needles of the chromic ribbon gut sling around the lower pole are passed through the quadratus lumborum muscle. It is observed that this fixation puts the ureter on the stretch, relieving the kink of the ureter which formerly existed.

After a chromic ribbon gut strip is thus placed around each pole of the kidney, a slit is made in the capsule at the summit of the cortex and it is then stripped back so that a raw surface is exposed.

The needles attached to the sling of chromic ribbon gut around the upper pole of the kidney are then inserted just above the border of the twelfth rib as far back as possible and about one inch apart. These ends are drawn through tightly, bringing the kidney and its partly denuded cortex up to the body wall. The ends are tied and the fixed needles are cut away.

The ends of the chromic ribbon gut which hold the lower pole in a similar sling are passed through the quadratus lumborum muscle at an appropriate place and tied, the needle studded ends then being cut away.

The wound is closed in layers in the usual manner.

This operative procedure has been very successful in our hands, and while sufficient time has not elapsed to make it possible to render a final opinion as to the ultimate results, the experimental work proves conclusively that there is no damage to the kidney, which stays where it is placed.

RUPTURE OF THE KIDNEY

During the delivery of a dog's kidney in one of our operations that organ was accidentally ruptured. A thin piece of fat was applied to the ruptured portion and fixed by plain ribbon gut held in position by being passed through straps made in the fibrous kidney capsule.

The dog was sacrificed fourteen days later and postmortem examination revealed the fact that the ruptured portion had healed perfectly, incorporating the fat in the scar in a satisfactory manner. There was no evidence of extravasation of urine or other untoward result.

Five other dogs were then operated upon and brief protocols of their course follow:

Dog S-10.—Traumatic rupture of the left kidney July 10, 1933; sacrificed August 12, 1933. Usual exposure. With a spatula considerable damage was done

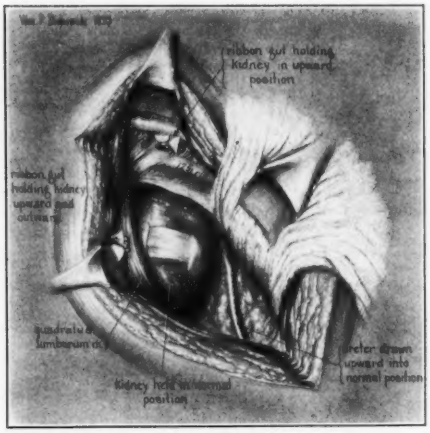
ribbon gut holding kidney in upward position
ribbon gut holding kidney upward and outward
quadratus lumborum
ureter drawn upward into normal position
kidney held in normal position

Fig. 7

Fixation is completed and the ureter is drawn upward into normal position.

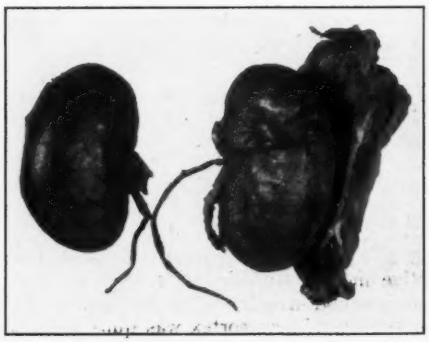

Fig. 8

Nephropexy performed May 11, 1933. Animal sacrificed July 28, 1933. The kidney was firmly fixed in the position it was placed in at the time of operation. The marks of the position of the ribbon gut could be made out, but none of the chromic ribbon gut could be actually identified. The control kidney shown at the left has the same size and appearance as the kidney operated upon. Dog S C O 5.

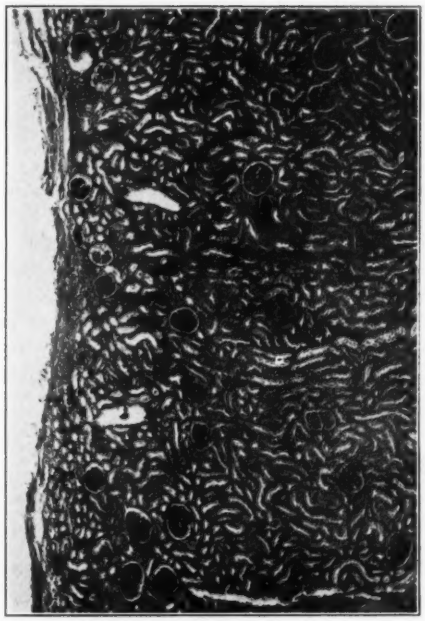

Fig. 9

Photomicrograph taken at the site at which the tape had been placed. It shows hardly any appreciable compression of renal tubules and a few plasma cells and lymphocytes. The rest of the kidney substance is without significant change. The gross specimen showed the kidney with excellent fixation to the body wall. The longitudinal section shows how little gross deformity of the kidney and microscopic change occurs in the renal cortex when tape is properly placed. Dog S C O 50, Pathological No. 16342.

to the kidney cortex. Fat was placed in the ruptured portion of the kidney. Straps had been made in the capsule which was opened and the ribbon gut tied firmly. The wound was closed.

Autopsy shows the control kidney of normal size; the left also normal. Fat is incorporated in the thick scar. Ribbon gut is not discernible. The cut section shows fat to be incorporated as part of the capsule. The cortex under the scar is somewhat paler than usual. No destruction to the kidney is noted.

Dog C-48.—Traumatic rupture of the left kidney August 3, 1933; sacrificed August 12, 1933. Usual exposure. With a blunt instrument the kidney cortex was injured. Fat was placed in the ruptured portion of the kidney. Straps had been made in the opened capsule, ribbon gut threaded through it, tied firmly, and the wound closed.

Autopsy shows the control kidney slightly enlarged. The position of the ribbon gut is plainly visible after 9 days. In some places it is not observed.

Cut section shows some scar tissue and blanching of the kidney cortex under the injured portion only.

Dog S-9.—Traumatic rupture of the left kidney July 18, '33; animal sacrificed Aug. 10, '33. Usual exposure. With a blunt dissector kidney struck three times, which caused a marked subcapsular hematoma. There was maceration and a lateral tear. Fat was placed in the ruptured portion of the kidney. Straps had been made in the capsule, which was opened, ribbon gut threaded through it, tied firmly, and the wound closed.

At autopsy, the surface of the kidney showed some scarification. The ribbon gut was identified by a small groove.

In a cut section the cortex had about the same thickness as the control kidney. There was scar tissue at the site of trauma. The cortex was paler than usual.

Dog S-4.—Traumatic rupture of the left kidney July 12, 1933; sacrificed August 10, 1933. Usual exposure. With a blunt dissector the kidney was struck, causing only moderate subcapsular hematoma. There was profuse bleeding from the renal cortex. No fat was used. Straps were made in the capsule, ribbon gut threaded through them and the wound closed.

At autopsy, the kidney contracted down to about two-thirds normal size as compared with the control kidney. Ribbon gut was seen in position. There was a perinephritic inflammatory reaction.

In the cut section there was normal cortex except at the site of injury, where there was considerable scar tissue.

Dog 4.—Traumatic rupture of the left kidney July 26, 1933; sacrificed August 12, 1933. Usual exposure. The kidney was injured in the usual manner, causing

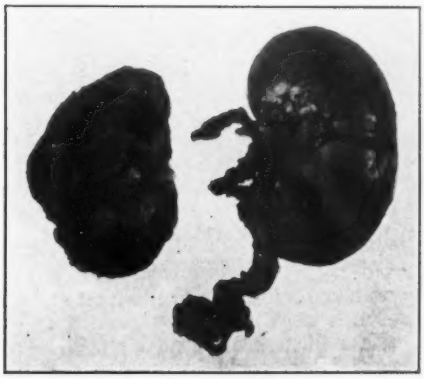

Fig. 10

Traumatic rupture of left kidney June 18, 1933. Sacrificed August 10, 1933. The control kidney is normal in size and appearance. The left kidney is about two-thirds the size of the other kidney. The left kidney is surrounded by a thick layer of fat. Upon dissecting this away the surface is seen to be irregular and scarified. The location of the ribbon gut is identified by a small groove in the surface of the kidney. Ends of the ribbon gut were easily discernible.

Bisection of the kidney shows a fairly normal kidney cortex in every part except in the upper and lower pole, where there is an excess of scar tissue. These are evidently the locations where the major portion of the trauma took place.

Comparing the cut sections of the traumatic kidney with the normal it is observed that the cortex is of about the same thickness, but it is much paler and is evidently the site of considerable scar tissue. This not only refers to the portion of the kidney injured, but to all parts of the injured kidney. Dog S 9.

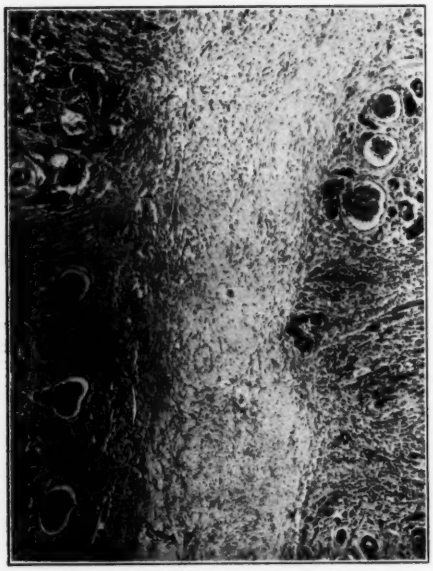

Fig. 11

This is a photomicrograph of a section taken directly through the injured portion of the left kidney. Several scarified areas are noted, but it is interesting to observe that there are many normal glomeruli present and apparently actively functioning. Dog S 9.

some hematoma. Straps were made in the capsule, ribbon gut threaded through it, and the wound closed.

At autopsy, ribbon gut over the lower pole was plainly visible. This kidney showed about 50 per cent damage.

The cut section showed normal cortex except at the site of injury. There was some scar tissue present. The cortex was slightly paler than normal.

SUMMARY OF EXPERIMENTAL FINDINGS

It was found impossible to rupture the fibrous capsule of a dog's kidney by striking its surface with a blunt instrument, although various degrees of injury could be done to the cortex of the kidney, depending upon the force used. The injuries produced varied from slight subcapsular hemorrhage to complete pulpefaction of that portion of the kidney cortex traumatized.

Upon opening the fibrous capsule following the injury, brisk bleeding always occurred and in the case of severe injury, serious hemorrhage was noted. In every case, this was readily controlled by applying thin particles of fat to the region of the bleeding points and repairing the wound by means of plain ribbon gut fixed in position by appropriate straps in the fibrous capsule.

In most of the experimental animals the loss of blood made intraperitoneal administration of normal saline solution necessary. All of the animals lived and it seemed most interesting that after a few days of lethargy they all recovered and not a single wound broke down or showed any evidence of extravasation at postmortem examination. The very satisfactory result seemed to be due to the fact that the tension produced by subcapsular hemorrhage was relieved by opening the fibrous capsule, and the actual bleeding was controlled by inserting bits of fat and approximating the ruptured portions by the use of plain ribbon gut properly applied.

After actual pulpefaction of a portion of the renal cortex, the tissue seems not to break down and produce abscess unless the fibrous capsule remains intact. In case the latter occurs the continued hemorrhage, the influence of the extravasted urine from the ruptured and macerated cortex, results in the ultimate rupture of the fibrous capsule, due to digestion, and abscess formation.

This usually occurs some time after the injury, which in itself may not have been considered severe.

A very thorough study by Delzell and Harrah of 11 cases of ruptured kidney occurring in our Hospital up to 1927 showed that it was found necessary to operate upon only 4 cases. Another patient, however, died before operation could be done, following an automobile accident. Another patient was operated upon and died.

Thus it was seen that of 11 cases only 5 were considered to be in need of an operation. On the other hand, the author has recently had a case which will be described below in detail, which demonstrates the desirability in certain cases of early operation, in order to save the kidney and to rescue the patient from serious infection and danger of death.

CASE REPORT*

M. C., age 19, a white male laborer, entered the Fitkin Hospital on October 19, 1930, complaining of pain and tenderness in the right abdomen and loin. He also gave a history of hematuria. His previous history is irrelevant. The present illness began on the afternoon of admission, at which time he was injured while playing football. Following the injury he passed bright red blood in his urine and felt weak and nauseated. A provisional diagnosis of ruptured kidney was made.

*This case is reported with the consent of Dr. J. D. Magee, of Asbury Park, New Jersey, who called the author to perform the final operation.

X-ray examination on the day after admission revealed a complete fracture of the right twelfth rib. The picture was suggestive of hemorrhage in and around the right kidney. Hematuria continued for four days and then cleared up.

Pain persisted with lessening severity and all was well until November 4, sixteen days after the original injury, at which time profuse hematuria occurred. It was necessary to catheterize the patient every six hours on account of the obstruction caused by clots in the bladder.

On November 6, eighteen days after the original injury, his red blood count was 3,780,000 and hemoglobin 70 per cent. A transfusion of 350 c. c. of citrated blood was administered.

After he had been free from hematuria for forty-eight hours following the transfusion, a brisk hemorrhage occurred into the bladder and for the first time, twenty days after the injury, a mass was made out in his right flank. The pain in this region was very severe.

On November 9, three weeks after the original traumatism, an operation was performed under spinal anesthesia. The kidney was exposed and found to be tremendously enlarged. Mobilization was impossible. A nephrotomy was performed. The capsule was opened near the lower pole and the cortex was found to be composed of macerated kidney tissue and blood clots. During the exploration of the kidney a tremendous hemorrhage occurred, which was finally controlled by much packing, which was applied tightly. The wound was closed around this packing and a transfusion immediately given.

The patient did poorly and was transfused four times as follows: four days after operation, on November 13, he received 350 c. c. of citrated blood. Again the next day he was given a similar amount and the following day he received 500 c. c. Two days later he was given 350 c. c. The result of these transfusions was satisfactory and the patient's general condition now warranted further surgical relief.

On November 18, nine days after the nephrotomy and thirty days after the football injury, the author was called in consultation and performed a nephrectomy upon the patient.

The wound was reopened and the packing carefully removed. The fragmented portions of the kidney were quickly isolated and during this procedure a massive gush of blood occurred that was controlled by prompt pressure with a large piece of gauze. The field was cleared and the bleeding point carefully approached from the side. The pack had to be removed entirely in order to approach the vessels of the pedicle. Part of the hemorrhage was controlled at the first attempt and complete hemostasis was accomplished at the second attempt. Gauze was lightly packed into the wound after removing all the fragments of kidney tissue which were partly necrotic. The clamps were left on. The wound was closed in the usual manner and a transfusion of 350 c. c. of citrated blood given on the table. The patient's condition was fair at the end of the operation.

His postoperative course was satisfactory. Drains were removed on November 22, four days after the second operation, and the clamps were loosened one notch. They were loosened completely the next day, and removed from the wound the following day.

The patient was allowed out of bed on December 9, twenty-one days after the nephrectomy and fifty-one days after the injury. He was discharged from the Hospital in good condition except for a slightly discharging sinus in the right loin on December 18, 1930.

It is our opinion that if this patient had bled a little more profusely at the beginning of his illness we would have operated within three or four days after the original trauma and saved the patient's kidney as well as his life.

DISCUSSION

Our experience with experimental operations upon rabbits and dogs using plain ribbon gut as a medium with which to close kidney wounds has proven to be entirely satisfactory. Fixing this material in a proper place, by threading it through straps in the fibrous capsule, is successful in maintaining the ribbon gut in the place desired for proper closure of the kidney wound or wounds.

Thin strips of fat inserted in the kidney wounds have been proven by animal experimentation and clinical observation upon human beings to be the most satisfactory material as an aid in hemostasis. Bits of muscle have also been utilized, but these are not nearly so effective in causing a cessation of kidney cortical bleeding.*

Microscopic studies demonstrate the thoroughness with which small particles of fat are incorporated in the healed wounds of the kidney. Large pieces of fat also may be included in the wound, but small ones are just as effective and are more easily absorbed by the healing kidney.

The ribbon gut properly tied around the kidney causes no pressure necrosis and postmortem specimens of animal kidneys show conclusively that there is no destruction to the kidney such as one sees when needles are passed through the cortical substance in the usual manner.

Nephropexy is perfectly performed by using three weeks chromic ribbon gut with needles attached to each end.

A sling of this material fixed in position around each pole of the kidney and tied firmly but not too tightly will be effective in holding the elevated kidney in whatever position it is placed at the operating table.

RUPTURE OF THE KIDNEY

It has been definitely proven by experimental and clinical observation that great destruction

*Particular attention is called to the excellent original work of Irving Koll, of Chicago, in this connection.

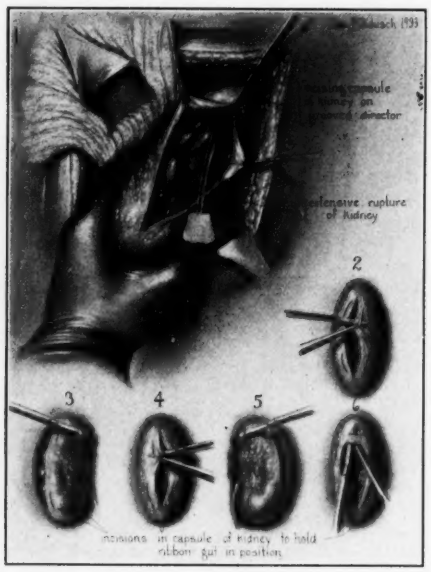

Fig. 12

(1) In rupture of the kidney the fibrous capsule is opened and clots are removed. (2) (3) (4) (5) (6) Shows the preparation of straps in the fibrous capsule for the reception of plain ribbon gut used in the repair of the injured kidney.

of the kidney may occur without rupture of the fibrous kidney capsule. As a matter of fact, pulpefaction of a large part of the kidney cortex may occur without any perirenal infiltration of either blood or urine until many days after the traumatism responsible for the lesion. This often may occur only after the fibrous capsule has been digested by the juices liberated under it.

Our experience with animals as well as the histories of many human cases lead us to suggest that every case in which renal traumatism is suspected be immediately hospitalized and carefully observed. If blood continues to be passed in the urine longer than twenty-four hours, or if there is lassitude, fever, rapid pulse or any of the ordinary evidences of absorption, an exploratory operation is recommended.

Upon exposure if subcapsular hemorrhage, evidence of laceration of the kidney cortex, or any other traumatism is noted, it is advisable to open the kidney capsule and drain the damaged portion by means of a soft rubber tube or in less severely traumatized cases by means of a Penrose drain. Bleeding, if it is still persistent, may then be controlled by inserting small bits of fat and fixing them in position by tying ribbon gut around the kidney and over the affected portions. The gut may be fixed in any desired position by means of three or four straps made in the fibrous kidney capsule.

In none of our cases thus treated has there resulted a death, nor has there been a persistent urinary fistula. On the other hand, in cases where the kidney capsule has not been opened and the traumatized area drained as in the case of "M. C." here reported, a complete destruction of the kidney has resulted which also became a great menace to the patient's life and except for prompt and efficient surgery would have resulted in death from hemorrhage and infection.

CONCLUSIONS

(1) Animal experimentation and clinical experience based upon observation at the operating table, functional tests after operations, pyelographic and microscopic studies, prove that:

(a) Hemostasis is most satisfactorily accomplished by tying ribbon gut around kidneys subjected to nephrotomy.

(b) There is perfect healing and apposition of the parts.

(c) There is the slightest amount of distortion of the kidney pelvis.

(d) There is little if any diminution of function in kidneys thus treated.

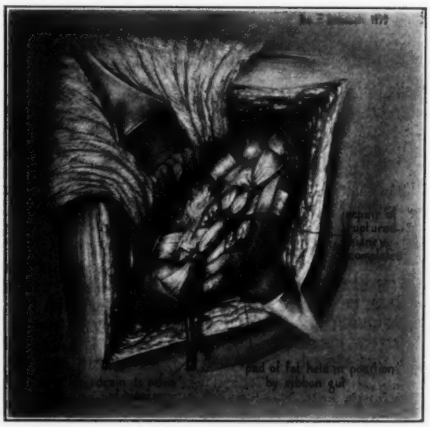

Fig. 13

Illustration shows a tube inserted into the kidney pelvis for drainage. Small particles of fat have been introduced into the injured cortex for the purpose of controlling the hemorrhage and the ribbon gut is tied, completing the repair of the injury.

(2) Nephropexy accomplished by the use of chromic ribbon gut as here described is a perfectly satisfactory method of operation in suitable cases.

(3) Experimental studies and clinical observation of rupture of the kidney convince the author that:

(a) Every case of renal traumatism sufficiently severe to cause hematuria or pain in the kidney should be hospitalized.

(b) Every case should be explored within twenty-four hours if the hematuria continues.

(c) Rarely does renal traumatism cause primary rupture of the fibrous capsule, although this structure may be digested by the ferments released by traumatism to the cortical substance resulting in perinephritis, infiltration of urine and pus and in many cases complete destruction of the kidney and menace to the life of the patient.

(d) The operation of choice in rupture of the kidney is control of hemorrhage and repair of the lacerated portion of the cortex by means of ribbon gut properly applied. Drainage is accomplished by means of soft rubber tubes.

(4) Fat is much superior to muscle or any other bodily tissue as an aid to the control of hemorrhage of the kidney cortex.

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CLINICAL OBSERVATIONS ON THE REDUNDANT COLON (DOLICHOCOLON)*

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Much interest has been manifested in recent years in the anomaly known as redundant colon or dolichocolon. This condition is far more common than has hitherto been generally recognized and is associated with a train of symptoms which are frequently misinterpreted. Since the diagnosis of this affection can only be arrived at with certainty by means of roentgen ray studies, it is only within recent years that its actual significance has become fully established.

The redundant colon represents an unusually lengthened large bowel folded up upon itself, forming extra loops, tortuosities and kinks, which may on this account interfere with its normal function. White[1] has aptly described this colon as "one too long for its owner or too long for the individual abdomen."

The redundancy may involve the entire colon or it may be limited to certain areas as the hepatic flexure, transverse colon, splenic flexure, but the distal colon especially in the region of the sigmoid is the most commonly affected.

Up to the time when the roentgen ray was first utilized for diagnostic purposes, this condition was observed now and then at autopsy or at operation. Fleischmann,[2] in 1815, and Monterossi,[3] in 1820, noted in the course of their autopsies the displaced position of the colon due to its increased length. These observations were confirmed later by Kuttner,[4] Gruber,[5] Treves,[6] Walther,[7] and Bryant.[8]

*Read in Section on Gastroenterology, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

*From the Gastroenterological Clinic of the Department of Medicine, University of Maryland, Baltimore.

Various surgeons, notably Roux,[9] Shober,[10] Duval,[11] Black[12] and Leveuf,[13] have likewise called attention to this condition observed at operation.

In many of the early descriptions of the redundant colon the symptomatology was largely intermingled with that of volvulus, Hirschsprung's disease and other conditions.

However, as the result of roentgenological studies, this affection has been most carefully investigated and a knowledge of its symptomatology more satisfactorily obtained. The first roentgenological description was given by Kienbock.[14] The first complete study of this condition, however, was published by Lardennois and Aubourg,[15] who are likewise responsible for the term "dolichocolon." Since then, numerous publications have appeared mainly in the English and French literature covering various phases of this subject both from a radiological and clinical standpoint. Among these are the articles of Siciliano,[16] Belot,[17] Kantor,[18] White,[1] Murray,[19] Slesinger,[20] Moller,[21] Larrimore,[22] Hecker, Grunwald and Kuhlmann,[23] Gauss,[24] Bush,[25] Reichenecker,[26] Strauss[27] and Bensaude and Monod,[28] Chiray, Loman and Wahl,[29] and La Rochelle and Smith.[30]

We have selected 50 cases of redundant colon as the basis of this study; in all of these the diagnosis was finally arrived at and confirmed following a complete investigation.

Etiology.—Authorities differ as to the frequency of colonic redundancy. According to White, it is observed in from 4 to 5 per cent of patients affected with digestive disturbances (two-thirds of the group being males); Kantor found it in 10 per cent of his cases, equally divided between males and females; Strauss in 8 per cent, Larrimore in 18 per cent, and Bryant in 15 per cent. In our experience it occurred in about 10 per cent equally divided between males and females (24 males and 26 females); the ages ranged between one month and 76 years.

Contrary to the view formerly held by certain authorities that the redundant colon occurs more frequently in the asthenic, visceroptotic type, it is now generally conceded that it is equally common in the asthenic well built individual and this conclusion is quite in accord with our experience. There can be no question, however, that it may be familial in origin. Bensaude, as well as Chiray, Loman and Wahl, produced evidence in this direction. The redundancy occurs most frequently in the distal portion of the colon, especially in the sigmoid area, and next in order in the descending and pelvic colon, the splenic flexure and terminal part of the transverse colon. Occasionally the entire colon is involved and even less frequently the hepatic flexure and ascending colon. When the latter are affected the symptoms are milder and less distinctive.

Of White's 43 cases, 16 occurred in the sigmoid, 8 in the splenic flexure; in 3 there was a general redundancy and in 16 the hepatic flexure was involved, while Kantor found that of 67 of his cases 27 occurred in the sigmoid, 14 in the splenic flexure, 20 in the descending and ileal colon, 3 in the transverse and 3 in the right colon.

Of our 50 cases, 21 were in the sigmoid, 9 in the splenic flexure, 2 in the hepatic flexure, 16 in the descending and pelvic colon, 1 in the transverse colon and in one there was a general redundancy.

It is of interest to note that due to the length and motility of the part involved, there is frequently a change in position of the intestinal loop. The most common variety is an enlarged sigmoid loop centrally placed, rising out of the pelvis, often forced into the cecal region, and then again into various parts of the abdomen. Redundancy in other parts of the colon likewise produces frequent changes in position and location. Indications of spastic contractions in various portions of the colon and kinks due to actual adhesions are often observed.

The stomach is occasionally deformed and displaced to the right due to pressure of the distended bowel. Other deformities of the stomach due to the same cause may likewise occur in the form of hour glass formation, rotation of the stomach and defects which are noted roentgenologically and which may lead to errors in diagnosis unless carefully interpreted.

Two theories have been proposed regarding the etiology of the redundant colon: that it is congenital or acquired. Both are probably correct. Most authorities, however, favor the congenital theory. It is quite true that a type exists which persists from birth without manifesting symptoms until late in life. *Figs. 4* and *5* illustrate two instances of redundant colon in childhood.

The acquired form is held to be produced as the result of disturbances of intestinal motility or inflammatory processes. According to White, the redundant colon "is occasionally acquired by overloading and stretching the sigmoid and transverse colon in chronic constipation." Lar-

Fig. 1
A redundant loop of the sigmoid.

dennois and Aubourg likewise maintain that colitis may initiate the process.

Symptomatology.—It is important in considering the symptomatology of the redundant colon to recognize the fact that it is not alone dependent upon the exact length of the affected bowel, but far more upon its disturbance in function; for as Bryant has clearly demonstrated, there is normally considerable variation in this direction. It has been shown that not until function is disturbed are symptoms manifested. On this account, the redundant colon may be present in many instances in a latent state from birth and symptoms may not develop at all or not until adult life.

On the other hand, the longer the loop and the greater the loss of tonicity of the musculature of the bowel the greater is the possibility for the production of symptoms.

The most pronounced symptom is constipation, which is persistent, often dating as far back as birth, and not uncommonly associated with pain later on in life. There are frequently long intervals between stools, at times five to ten days, following which the patient may be quite comfortable and apparently in good health. The constant employment of cathartics as well as enemata is required, and as time proceeds these become less and less effective. The feces are dry, hard and of the scybalous type, but when the bowel is completely emptied at long intervals the stools are evacuated in copious amounts of large caliber pointing to an atonic state.

Inasmuch as a loop may become twisted or overfull at irregular intervals with a tendency to the production of a temporary obstruction, constipation as well as the other signs of this condition may occur only at intervals. Chiray, Loman and Wahl have commented upon the peculiar disappearance of symptoms for a considerable period of time as the result of general measures such as change of scene or a vacation away from home. This is probably due to the improvement occurring in the tone of the bowel as the result of an upbuilding of the nervous system. Constipation was present in 69 per cent of Kantor's cases and in 70 per cent of White's. It was present in 68 per cent of our cases. Gaseous distention and fullness producing distress of more or less severity are frequent. The patient often complains of this condition at one part of the abdomen or another, not uncommonly corresponding with the loop involved. The attacks of colic may become violent, are often associated with constipation and are the result of partial intestinal obstruction. At times attacks of gaseous distention alternate with constipation. The colonic distention and colic are frequently relieved by the expulsion of gas, which may be induced by change in posture of the patient. Aërophagia is not uncommonly present, but the distention due to this condi-

Fig. 2
Redundancy of the lower descending colon.

Fig. 3

Roentgenogram showing a marked looping and displacement of the splenic flexure; also a small loop in the sigmoid colon.

tion differs markedly, both in situation and degree, from that occurring with the redundant colon, being far less intense and more constant.

The gas expelled rectally is odorless or foul, depending largely upon the length of its retention or upon the pathological changes which have taken place in the redundant sigmoid. Gaseous distention occurred in 70 per cent of Kantor's cases, in 63 per cent of White's, and in 58 per cent of ours.

Pain is an important symptom and occurs with varying degrees of intensity; it may be absent or at times it is mild and at others severe. It may be general, extending over the entire abdomen, or localized in certain areas, often confined to the redundant loop. It is more frequent on the left side, though it may be reflected to the right or into the epigastrium and back. An occasional volvulus involving the sigmoid has been observed. The acute attacks which may be preceded by an increase in constipation are often extremely violent and may persist for a varying period of time, producing a sensation of torsion. After subsiding, they are usually followed by a localized tenderness in the affected area. These attacks are often accompanied by nausea and vomiting as well as a distention which is frequently localized. The facial expression of the patient reveals great suffering. The pains may be of such a type as to simulate cholecystitis, appendicitis or even cardiac disease. The pain is due to distention or partial or actual obstruction, together with spasm; as well as to the pathological changes that have occurred within the affected loop.

Abdominal pain was present in 52 per cent of Kantor's cases, in 62 per cent of White's and in 54 per cent of ours.

Associated with the foregoing symptoms, or occurring alone, are manifestations of a general type, toxic or nervous in character, but by no means characteristic of the redundant colon. These occur in the form of indigestion with aërophagia or with diarrhea, palpitation, general weakness, exhaustion and occasionally in the form of mild febrile attacks. Such symptoms occurred in 84 per cent of our cases. Chiray, Loman and Wahl, in their very elaborate study of the dolichocolon, distinguished in addition eleven groups of redundant colon from a clinical standpoint.

(1) *Colitis Type.*—In this form there is an associated colitis so severe as to resist all treatment. Diarrhea is present and digestive symptoms develop as the result of allergic reactions to certain foods.

(2) *Dyspeptic Type.* — The symptoms are

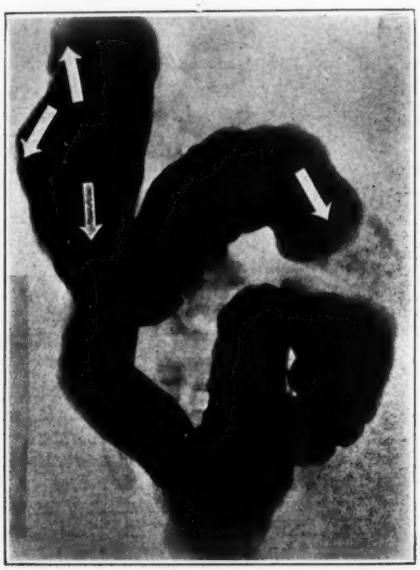

Fig. 4

A lengthened colon in a child aged one month. Note the extra loop in the hepatic flexure and splenic flexure area. The roentgenogram illustrates the overshadowing of the loops.

Fig. 5
A markedly long colon in a child aged three months. Note the redundant loops at arrows.

largely of a dyspeptic character, consisting of nausea, vomiting, eructations, foul breath and discomfort in the epigastrium associated with pylorospasm and abdominal distention.

(3) *Cholecystic.*—In this type symptoms referable to the gallbladder are prominent. These are intermittent and are associated with a slight icterus and pain in the gallbladder area. A careful examination reveals, however, that the liver and gallbladder are normal and that the symptoms are actually produced by the colonic redundancy.

(4) *Enterorenal.*—In this type, pyelitis complicates the condition and only by means of radiological studies is it possible to discover the primary affection.

(5) *Intestinal Stasis with Right-sided Pericolitis.*—This type, in a measure, resembles appendicitis. On palpation, a tenderness can be detected over McBurney's area, but the absence of nausea, vomiting, fever and other signs of acute appendicitis render the diagnosis less difficult than in the chronic forms. Chronic constipation and other signs indicating the presence of the redundant colon must be considered in arriving at the diagnosis.

(6) *Pseudo-Tumor.*—In this type a tumor manifests itself on palpation usually in the left iliac fossa. This tumor disappears following a complete bowel evacuation. The distinctive feature is the intermittent appearance of the tumor.

(7) *Rectal.*—The rectum being involved in these cases by pressure or otherwise, symptoms predominantly referable to this region are produced.

(8) *Hemorrhagic and Anemic Form.*—In this type hemorrhages occur which may be either of gastric or intestinal origin. Bleeding may be profuse and may closely resemble that of peptic ulcer. It may lead to a profound anemia.

(9) *Types in Which General and Nervous Symptoms Predominate.*—This form occurs largely in young individuals of extremely nervous and neurathenic temperament and is associated with vague abdominal symptoms. The colonic redundancy can be disclosed in these instances only following intensive roentgenological studies.

(10) *"Fruste" or Latent Forms.*—This type manifests itself in the form of chronic constipation and may represent the initial stages of the severer forms or may remain latent until late in adult life and symptoms may occur only following functional disturbance of the affected loop.

(11) *Infantile and Familial Forms.*—This type can be recognized in early infancy and may likewise be of familial origin.

Complications. — Among the complications arising as the result of colonic redundancy are obstructions of the bowel (volvulus), inflammatory lesions within or without the bowel (colitis; pericolitis; adhesions) followed occasionally by suppurative processes, intestinal hemorrhage and secondary anemia.

Associated lesions likewise occur at times as appendicitis, cholecystitis, peptic ulcer, diverticulitis, or colonic cancer.

In our series partial obstruction of a mild or high grade occurred in 19 instances, colitis in 8, intestinal hemorrhage in 1, marked enteroptosis in 11, acute appendicitis in 3, chronic appendicitis in 10, cholecystitis in 2, and peptic ulcer in 3.

Diagnosis.—The diagnosis of redundant colon is almost entirely dependent upon roentgenological investigation. The symptoms in themselves are by no means conclusive and the diagnosis cannot be made upon these alone, but following x-ray studies they may be of considerable value as confirmatory evidence.

The roentgen ray examination includes a study following a barium meal and enema. The meal reveals more clearly and definitely the

functional activity of the bowels, the enema, its anatomical relation and form. Both methods are equally valuable and indispensable. A scout examination made preceding the administration of the barium meal may reveal an extensive accumulation of gas most frequently in the upper left quadrant or in other regions of the abdomen and occasionally the affected loop may be outlined by this procedure.

A study of the colon following the barium meal, after a period of 24 hours, will not reveal the presence of this anomaly in most instances. This is especially true of the milder forms of the condition, but in the markedly redundant bowel this method of examination will often show an accumulation of barium or gas in the distended loop. This method is, however, essential in determining the function of the bowel and is an important procedure to follow as a routine in all instances. It does not, however, by any means present a complete picture of the condition, inasmuch as in most instances the distribution of the barium is irregular and scattered, producing an incomplete filling of the bowel.

Following the barium meal, displacement and deformities of the stomach may occasionally be noted and unless the investigation is thoroughly completed may lead to serious errors in diagnosis. The stomach may be displaced to the right or may be rotated or may present an hour glass or cascade appearance. It may be dome-shaped or the pylorus may be directed backward. Pressure defects in the stomach or duodenum may also occasionally be produced, which may lead to an erroneous diagnosis of ulcer or even carcinoma. However, on subsequent re-examination marked alterations in these findings are at once observed not only in the situation of the stomach, but likewise in its deformities and motility.

These changes while in progress can best be detected under the fluoroscope.

The barium enema examination, on the other hand, is the method of choice and is the most satisfactory procedure in the examination of the bowel for the detection of this anomaly. The fluoroscopic procedure is by far the most ideal method of studying this condition. In this examination the extra loops that are overshadowed can be more clearly brought into view. As the most common sites of extra looping of the bowel are the flexures and the pelvic colon, overshadowing is extremely common and on this account the fluoroscopic examination affords a most satisfactory method for the study of these areas. The overshadowing of these segments often produces a picture resembling a normal colon. Hence the condition may be entirely overlooked by the roentgenologist. Displacement of the segments of the bowel is not infrequent, but these are most readily detected during the roentgen study. Further detailed study of the redundant loops may be more readily made by the introduction of air into the bowel.

The unusual length of the bowel, distention, abnormal accumulation of gas and extra looping are the four cardinal roentgen signs in the diagnosis of the redundant colon (*Figs. 1* and *2*).

The diagnosis of redundant colon is dependent upon the visualization of the involved loop, its site, extent, variability and the changes which it undergoes. This necessitates examinations following both the barium meal and the enema. In general, more or less accumulation of barium is observed in the loops associated with gas. This accumulation may be quite extensive, but usually varies from time to time. A characteristic finding is a change in location of the loop occupying, as it does, various positions as the result of pressure from its contents and presenting deformities of various forms. Thus the enlarged sigmoid loop may rise out of the pelvis and then force itself to the right over the cecum and again in the mid-abdomen. It may even produce a double loop at the splenic or hepatic flexures.

The degree of spasticity of the loop is likewise determined by the facility with which it distends and contracts. Adhesions as well as intercurrent affections may be determined by means of roentgenological studies. The presence of colitis, diverticulitis or carcinoma of the bowel may also be revealed by this method.

It is of interest to note that the redundant colon may necessitate the use of an unusual amount of barium because of its extra length, greater caliber and atony which is produced by the long-standing distention. This fact in itself should give a clue as to the possibility of the presence of this condition. The extra looping may produce bizarre appearances of the colon, such as is noted in *Fig. 3*.

A study following the evacuation of the bowel is another important procedure to be followed. Immediately after completion of the examination following the colon enema the bowel is evacuated and again studied. This is an important step which should be carried out routinely to determine the level of stasis. It will be noted

that in most instances of the anomaly, following this procedure, the distended loops of the bowel interfere with the normal function to a greater or less extent, depending upon the tonicity, kinking and size of the loops.

In the general physical examination no very definite evidence of the presence of the redundant colon is ordinarily obtained. However, in the acute stage localized distention of the bowel or the presence of an intermittent tumor may be detected. Rarely peristaltic waves may be observed over the distended loop.

The examination of the stool furnishes but slight direct evidence of this affection. The stools are ordinarily fragmentary, scybalous and dry, followed at varying periods by profuse movements of large caliber. They are often fermented, foul in odor, may contain mucus and the test for occult blood is frequently positive. Rectal examination rarely furnishes information of importance.

The diagnosis of the redundant colon must be based largely upon a roentgenological study in addition to the clinical evidence already presented.

The following abstracted history presents the typical features of a marked case of redundant colon:

A. P., a man of 33 years, had been affected with constipation since infancy. In his boyhood days he was constantly disturbed and on this account was forced to take purgatives and enemas as far back as he could remember. The constipation was far more aggravated at certain times than at others and with it he suffered abdominal pain and distention. He could distinctly remember certain periods between his ninth and fourteenth years when three to four days passed without bowel movements in spite of his usual remedies and during this time he suffered great pain. However, there were periods extending at times over three or four years during which he was more or less comfortable and was able to secure movements more easily though never without active measures. Following his twenty-second year the constipation increased and distention and pain became more frequent and even violent at times, until bowel movements were secured with the greatest difficulty. During some of these attacks the symptoms simulated those of acute appendicitis, at others cholecystitis, at still others intestinal obstruction, and more than once was operation contemplated, but movements of the bowels were finally secured with relief.

On examination during an attack the abdomen was found markedly distended in the region of the lower left quadrant; there were paroxysmal attacks of pain, especially in this region, with tenderness, extreme nausea and vomiting, great weakness and exhaustion but no fever. There was a leukocytosis of 10,000. The diagnosis of obstruction due to adhesions or volvulus was made, but following a number of enemas the bowels were moved, large amounts of gas expelled and the patient was relieved.

Following recovery from the acute attack a complete examination was undertaken. The patient appeared in perfect comfort, though no bowel evacuation had occurred for two days.

A physical examination presented no abnormalities of the heart or lungs. The blood pressure was 118/80. The abdomen was somewhat distended in the lower left quadrant and slightly tender in this region. An examination of the gastric contents showed a normal acidity. The stool passed two days previously was hard and scybalous and was surrounded with mucus. It contained no visible blood and the test for occult blood was negative.

A roentgen ray study was undertaken both following a barium meal and enema. The stomach was found displaced to the right and a defect was noted at the pylorus, which was, however, inconstant. A large sigmoid loop was observed just above the pelvis on the left side which gradually altered its position to the right side and finally to the upper left quadrant. This was undoubtedly the distended sigmoid loop of a redundant colon and the diagnosis was definitely established.

Differential Diagnosis.—The diagnosis and differential diagnosis is simple in most instances, but when complications arise this may become extremely difficult, especially when acute symptoms present themselves as in the initial attack before roentgenological studies have been undertaken.

In the differential diagnosis of this affection intestinal obstruction, appendicitis, cholecystitis, renal colic associated with paralytic ileus and colonic carcinoma must be considered. The symtomatology of these affections, however, together with complete roentgenological and clinical studies, will usually lead to correct conclusions. It is extremely important in the acute attacks to arrive at an early decision in order to avoid unnecessary surgical procedures.

Treatment.—The object of treatment is to overcome the symptoms produced by this affection by restoring the normal function of the bowel as far as this is possible. Many patients may not suffer discomfort for long periods and may therefore require little treatment.

In the acute attacks hot applications should be applied to the abdomen and enemata administered in order to secure adequate bowel evacuations. These should consist of bicarbonate of soda solution or olive oil. Belladonna or atropine should be prescribed in adequate doses and, if necessary, hypodermic injections of pituitrin should be given.

In the general treatment of the patient attention must be directed to the diet. This must be adequate, mixed, rich in vitamins,, bulky in type, but bland in form, consisting largely of pureed vegetables and stewed fruits in order to

stimulate the bowel movements. The constipation is best overcome by adequate doses of mineral oil by mouth and retention oil enemata at night. Drastic purges or enemata must be avoided. Kantor maintains that volvulus has been induced by violent efforts at purgation. Abdominal exercise, massage and the employment of the infra-red rays over the abdomen are helpful procedures. Belladonna and atropine have been recommended. Under conservative medical treatment most patients make at least a satisfactory clinical recovery, even in moderately severe or severe instances. The function of the colon is restored and by overcoming the tendency to constipation, associated inflammatory processes are relieved. Surgery should not be attempted unless serious obstructive signs occur as in volvulus, actual ileus, or such complications as perisigmoidal abscess.

The operation of left lumbar ramisection (sympathectomy) first recommended by Wade and Royle[31] and since by others for the treatment of Hirschsprung's disease has been suggested by Chiray, Loman and Wahl as a measure for possible relief in intractable forms of redundant colon.

SUMMARY

The redundant colon is far more common than is usually recognized. It is often overlooked or mistaken for other affections. Only by most careful roentgenological studies can the diagnosis be definitely established. The most common symptoms noted are constipation of a severe type, distention and abdominal pain, though the condition may remain latent for long periods. The possibility of this affection must be considered in all chronic abdominal conditions associated with the symptoms described. The treatment is medical, and sugery should only be considered when serious obstructive complications occur.

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DISCUSSION (*Abstract*)

Dr. Dewey Davis, Richmond, Va.—Drs. Friedenwald and Feldman have presented to you a condition which justifies more attention from the medical profession. We are so prone to center our thoughts on local disease in the abdomen, such as appendicitis or cholecystitis, that we may fail to realize that disturbances of the colon, either of spastic or atonic nature, are the source of symptoms which are attributed to other organs. For this reason operative procedures often fail to relieve the patient.

I have been particularly interested in the dilatation and redundancy of the colons of certain individuals suffering from chronic rheumatoid arthritis. Several observers have reported on this finding. It is indeed striking to note the improvement in some of these colons following a diet rich in vitamins with low carbohydrate content and with adequate measures to control the constipation which is usually present.

Dr. Friedenwald (closing).—This anomaly, the redundant colon, has attracted considerable attention in recent years. It gives rise to a symptomatology the diagnosis of which should not be overlooked. While it was formerly considered to be observed only in the asthenic visceroptotic type of individual it is really found equally commonly in the asthenic, well built individual. The condition is observed largely in the sigmoid and descending and pelvic colon. It is interesting to note that the symptoms produced are not dependent alone upon the exact length of the affected bowel, but far more upon its disturbance of function; and symptoms are not actually produced until its function is interfered with. It is, therefore, quite possible that the redundant colon may be present in a latent state from birth and symptoms may not develop until late in life. However, the longer the loop the more likely are symptoms to occur. The symptoms of persistent constipation with tendencies to temporary obstruction, abdominal colic and colonic distention and pains of varying intensity are most common. The condition may simulate cholecystitis, appendicitis and other diseases. The diagnosis is largely dependent upon the roentgenological investigation, which includes the barium meal and enema. Treatment must be directed to diet, which should be adequate, mixed and rich in vitamins, containing food having a tendency to stimulate bowel activity. Mineral oil by mouth and retention oil enemata at night are valuable. Abdominal exercise is useful. If the condition is not too aggravated, a clinical recovery under medical measures is not unusual. In more severe and intractable forms, left lumbar ramisection (sympathectomy) is indicated.

OBSERVATIONS ON NATURALLY INDUCED MALARIA*

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The discovery of the manner of malaria transmission stimulated the prosecution of a vast amount of research on this problem, which, owing to the complexity arising from regional and local factors, still commands attention. This progress, however, initiated comparatively little advance in the study of problems presented by clinical malaria, a circumstance attributable to the non-availability of an experimental animal reliably susceptible to the parasites of human infections. Consequently progress in our knowledge of malaria has seriously lagged behind that of other infections. An impetus, which may supply this deficiency, has been given by the now well recognized practice of employing naturally induced malaria in the therapy of paresis and other related affections of the central nervous system of syphilitic origin, which permits the inoculation of selected subjects under controlled conditions.

Our knowledge of the phenomena associated with the evolution of any of the self-limited infectious diseases such as typhoid is very comprehensive and is attributable to the lack of means to impose any artificial limitation. On the other hand, since the recognition of the value of cinchona and its derivatives, physicians have felt an obligation in malaria cases to interrupt the natural evolution of the infection in an effort to effect a cure. Consequently our understanding of the clinical course of malaria is less comprehensive. Here again naturally induced malaria therapy affords an opportunity to supply a deficiency.

We speak of naturally induced malaria as contrasted with artificially induced malaria. By the latter term is designated the attack of malaria induced in a recipient by the transfer of blood from a malarious donor, either by intravenous, intramuscular or subcutaneous injection. The parasites which develop in the recipient represent the direct continuation of the schizogonous forms present in the donor. The previous term designates the attack initiated by the introduction of the mature cells of the sporogonous cycle (that is, sporozoites) effected either by natural inoculation by artificially infected anopheline mosquitoes, or artificial inoculation with a suspension of sporozoites derived from such mosquitoes. It thus corresponds in origin with the autochthonous disease. In view of this circumstance, observations, clinical or otherwise, on naturally induced cases must have a significance that cannot be attributed to cases artificially induced.

While the employment of naturally induced malaria presents technical difficulties, which in certain places may prevent it from supplanting the practice of artificial inoculation, it does present certain advantages that are of sufficient consequence to outweigh the difficulties. Thus mosquito inoculations practically exclude the possibility of introducing pyogenic and other extraneous organisms. They avoid the necessity of introducing into a patient of one race blood of an individual of another race. They generally assure a clinical course of longer duration, with a longer latent period, both of which are important considerations, since the benefits from an attack are frequently proportional to its duration and the continued presence of the parasites. Parasite strains are available which can be well borne by selected patients, while the attacks are readily interrupted, or terminated if necessary in the interest of the patient. Suitably controlled mosquito inoculations give a higher proportion of takes than any other except intravenous inoculations with blood. They further do not inconvenience the patient, avoid the necessity for blood typing and eliminate the reaction which may follow the introduction of incompatible blood.

It is perhaps unfortunate that the word malaria is so extensively employed, since many lose sight of the fact that this is a non-specific collective noun, which includes in its scope at least three specifically different human diseases. It is true that they are all produced by very closely related parasites, are transmitted in a similar manner and exert a very similar clinical effect in the body. But, on the other hand, they differ among themselves. Distinctions can be noted in the epidemiology, symptomatology and response to therapeutic agents sufficiently marked to necessitate their distinct and specific differentiation before the management of a given case can be intelligently directed. We must think of tertian malaria (*Plasmodium vivax*),

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*Read in General Clinical Session, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

*The studies and observations on which this paper is based were conducted with the support and under the auspices of the International Health Division of the Rockefeller Foundation, in cooperation with the Florida State Board of Health and the Florida State Hospital.

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quartan malaria (*P. malariae*) and estivo-autumnal (*P. falciparum*) instead.

Our studies of naturally induced malaria have been carried on in the Florida State Hospital, with the collaboration of the medical staff, thereby making malaria therapy available to patients in that institution. It is a pleasure to acknowledge the sympathetic interest manifested and the assistance given by Dr. J. H. Pound, the chief physician, as well as by our mutual colleagues on the hospital staff. These studies have been continued over a period of two years, and to June of the current year include 109 successful inoculations with benign tertian, 9 with malignant tertian, and 5 with quartan. Apart from the results of certain propagative inoculations done for therapeutic purposes, but planned in such a manner that the results would have a definite experimental significance, we do not consider it desirable at this time to present our clinical observations in other than a provisional manner, as our series of case histories at present is neither sufficiently broad or adequately analyzed.

The principal requisite for the prosecution of naturally induced malaria therapy throughout the year is a sufficient supply of anopheline mosquitoes, preferably secured by rearing. Until the development of a technic which permitted the maintenance of a perpetuating colony of these insects, such continuity was impossible. We have successfully propagated *Anopheles quadrimaculatus* in an insectary for the past two years, securing an adequate supply of vigorous, uninfected mosquitoes at all times.

A further requisite is a continuous supply of patients for whom malaria therapy is indicated, in whom the strains of malaria parasites may be successively propagated. Consequently such services can only be organized in conjunction with mental hospitals.

In order to verify the status of our inoculations, all anopheline mosquitoes employed are immediately dissected and examined to determine the presence of sporozoites in their salivary glands. If none is found, the applications are repeated until one or more infected mosquitoes have actually been applied.

A description of the technic required for the rearing of anopheline mosquitoes, for the infection of mosquitoes, their subsequent conservation and application and the management of the patients is too lengthy for inclusion here. Those interested are referred to the publications of the station.[1 2 3 4 5]

TERTIAN MALARIA

During the past two years we have had in our possession four strains of *P. vivax* of local origin. One of these has been continuously employed and has now gone through fourteen consecutive anopheline-human passages. None of these four strains have possessed noteworthy virulence, although two, now discontinued, produced a definitely severer illness than did the others.

In 103 primary inoculations of white patients, 87 takes were secured. Of the 16 cases which were failures, 12 were later subjected to reinoculation, and takes were secured in all. We are thus led to believe that white persons who are not harboring a latent infection are probably invariably susceptible, while failures are attributable to deficiencies of the sporozoites.

Negroes, on the other hand, show a high degree of tolerance. Thus of 14 primary inoculations of negroes with this parasite, only 5 takes were secured. Of these five, only three presented any clinical reaction, a light fever not lasting more than six days with no recurrences. The others were transitorily blood positive. In none was the attack of sufficient duration to be of any therapeutic benefit. We have tried to infect negroes with very massive doses of sporozoites, as determined by the numbers of infected mosquitoes employed. Thus in one trial, twelve white controls to whom the mosquitoes were applied all became infected, while the negroes remained completely negative. Wishing to secure some idea as to whether the tolerance might be either acquired or racial, we arranged for the inoculation of a negro child five years of age who had hereditary lues. Daily blood examinations over several weeks prior to inoculation were consistently negative for malaria parasites. Inoculation by means of mosquitoes was unsuccessful, though white patients on whom the same mosquitoes were previously and subsequently applied contracted infection. The tolerance of negroes is relative, not absolute, as shown by the occasional successful, though short, infections induced.

At a temperature of 20° C., the parasite requires about 17 days to complete its sporogonous cycle (extrinsic incubation) in anophelines. The intrinsic incubation in our cases has never been less than 10 days in duration and only infrequently over 20 days. We have, however, observed periods as long as 85 and 97 days' duration. Its modal duration is 13 days (mean 15 days). In general it would ap-

pear that the duration of the incubation period is directly proportional to the dose of sporozoites received.

Biological races or strains of the parasite, morphologically indistinguishable, appear to exist within the species. Patients recovering from a clinical attack of tertian malaria acquire a tolerance to the strain of the parasite responsible for their attack, which prevents a successful reinoculation or superinfection with the same strain. This appears to persist as long as the infection remains latent, that is, as long as the patient is harboring the parasites, and appears to continue for at least a few weeks following their disappearance. On the other hand, a patient can be successfully inoculated with a different strain while still harboring the parasites of his first infection. The tolerance is homologous but not heterologous.

The clinical attack may present three different phases. One attack may exhibit all, or be limited to a single phase. When all phases are noted, the attack is initiated by a period of irregular remittent fever lasting from 3 to 5 days, during which no chills are experienced. This is succeeded by a period of quotidian intermittent fever which may last for three weeks or longer. This in turn may be followed by a period of tertian fever. Most commonly the onset begins with quotidian intermittent fever which persists throughout the course of the attack. Rarely the attack may consist of tertian fever alone. Not infrequently the tertian phase is succeeded not by spontaneous termination, but by a return of quotidian fever. While we are always prepared to interrupt an attack when the red count falls below 2 million and the hemoglobin below 40, we observe that when these figures are approximated, the patients usually experience a spontaneous remission. If the physical condition of the patient permits, it is always our desire that the attack continue to a spontaneous termination, as not only do the therapeutic benefits appear to be more marked, but we consider it desirable to have the infection run into the third week, as it is about this period that the earliest mental improvement is noted.

Quotidian fever would naturally appear attributable to 2 alternating schizogonous cycles of parasites. Such an occurrence has been ascribed to double infection, that is, inoculation on two successive days. We have only rarely applied mosquitoes on more than one day, nevertheless quotidian fever is the most common characteristic of the clinical attack.

Patients infected with tertian are, practically speaking, infectious for mosquitoes from the onset. We have infected mosquitoes which were applied to a patient on the third day after the first detection of parasites. Gametocyte production is more constant and abundant during the primary attack than during recurrences.

In general, the remittent fever would appear indicative of the highest susceptibility, quotidian fever of slightly lesser susceptibility, while tertian fever is suggestive of appreciable tolerance.

Splenomegaly is not detectable at the onset nor for several days thereafter. It is usually first observed between the fifth and tenth days.

In 52 per cent of our cases, parasites have been detected in thin smears before the first rise in temperature to 100° F., even as much as 6 days before the onset. In 18 per cent they were first discovered on the day of the first rise in temperature, and in 30 per cent they were discovered only subsequently. None of these examinations required over 30 minutes' time. In no case were the parasites at this time ever more than scanty, suggesting that in susceptible individuals the clinical attack is initiated by a very low density of parasites.

We are of the opinion that the parasite density at the onset of a clinical attack affords the best means available of differentiating the onset of a new infection from renewed activity of an old infection. This may be supplemented by examination for splenomegaly. Thus:

	Onset of New Attack	Onset of Recurrence
Parasites	Very scanty	More numerous
Splenomegaly	Not observable	May be observed

When the attacks have been allowed to progress for some time they are very amenable to the exhibition of quinine. Single doses given prior to an expected paroxysm, even of as small an amount as ten grains, are sufficient to check the paroxysms for several days. For termination of the infection we have employed a brief intensive course of quinine given after the method of Sinton[5] with very satisfactory results.

Our experience with recurrences in 87 primary white cases may be summarized as follows:

	Total Cases	Experiencing Further Activity Number	Per Cent
(A) Termination of primary attack			
(a) Spontaneous			
(1) Not later treated	35	20	57.2
(2) Treated later	18	0	.....
(b) Induced			
(1) Not later treated	12	11	91.6
(2) Treated later	21	2	9.5
(3) Atebrin	1	0	.....

(B) Termination of first recurrence			
(a) Spontaneous			
(1) Not later treated	12	7	58.
(2) Treated later	6	1	16.7
(3) Atebrin	2	1	50.
(b) Induced			
(1) Not later treated	4	1	25.
(2) Treated later	7	2	28.6
(3) Atebrin	2	1	50.
(C) Termination of second recurrence			
(a) Spontaneous			
(1) Not later treated	5	1	20.
(2) Treated later	3	0	.....
(3) Atebrin	1	0	.....
(b) Induced			
(1) Not later treated	2	1	50.
(2) Treated later	2	0	.....

It is interesting to note that the natural cure rates of untreated cases, following (a) spontaneous termination of the primary attack (Aal), and (b) following spontaneous termination of the first recurrence as well (Bal) are practically identical, namely, about 40 per cent. In other words, 40 per cent of tertian cases which spontaneously recover from the primary attack, will not experience a recurrence. Of those which experience one recurrence, 40 per cent will not experience a further recurrence. The benefit from withholding intensive treatment until the patient has acquired a tolerance (Aa2) is shown by the absence of recurrences in this group. More nearly similar to the conditions of practice are the groups Ab1 and Ab2. In the first, where only a few small doses of quinine were given, all patients experienced a recurrence, but when treatment was intensive, cures were high. These data suggest that from a practical standpoint, induced cure must depend upon the joint action of the body's defenses and medication.

After the passage of more than six months from the termination of the initial attack in all these 87 patients, renewed clinical activity was observed to have occurred after the following periods of time, namely:

In less than 8 weeks	31, or 35.7 per cent
In from 8 to 24 weeks	4, or 4.6 per cent
In over 24 weeks	2, or 2.3 per cent

Of the 87 white and 5 negro patients here considered, there have been nine deaths among the whites and none among the negroes. None of these deaths could be attributed to malaria therapy. We conclude that there is very little risk attached to the employment of tertian malaria in the therapy of selected adult white patients, particularly when the evolution of the infection is carefully followed.

ESTIVO-AUTUMNAL MALARIA

We cannot at present say a great deal about this type of malaria infection, as our experience is yet very limited. It is being employed in a guarded manner in order to make malaria therapy available to negro patients. We have encountered certain technical difficulties which have not as yet been overcome, that so far prevented our work from having the degree of precision which has developed in the employment of tertian. Our experience is so far limited to two strains of local origin.

We have found certain negroes to possess an appreciable resistance, apparently observable when inoculations with small doses of sporozoites are made. It is of much less frequent occurrence than that shown to tertian.

Mosquitoes incubating this parasite at a temperature of 20° C. complete the extrinsic incubation period in about 23 days. The intrinsic incubation period has varied between 8 and 15 days, averaging 11 days. No cases have shown the extreme duration sometimes seen with tertian.

Patients harboring a latent infection with a strain of this parasite possess a tolerance (homologous) to super-infection with the same strain. We have not as yet investigated the possibility of a heterologous tolerance.

The clinical attack presents the same phases as observed in tertian, which appear to have the same significance. Most attacks, however, appear to possess a potentiality for an accelerating evolution, which if unchecked might overwhelm the patient. This is manifested by a progressively ascending temperature in either the remittent or quotidian intermittent phase. This can be checked and controlled by administering quinine in ten-grain doses during any paroxysm when the temperature ascends above 104° F., repeating the dose within an hour if required. The repetition of this practice on two or three successive days has retarded the evolution of the infection sufficiently so that subsequent interference is rarely required. With this management we are enabled to permit the attacks to continue to spontaneous termination.

Gametocytes are not usually observed before the seventh to the tenth day of the attack, at a time when the density of the trophozoites is diminishing.

QUARTAN

Our experience with quartan malaria is still more limited. We have worked with two

strains, one of which is of local origin, and which has been carried through two successive human-anopheline passages. Our experience with this parasite does not suggest that it is well adapted for use in naturally induced malaria therapy, largely because the supply of infected mosquitoes cannot be frequently renewed.

We have so far inoculated four whites and two negroes by means of proven mosquitoes, all of whom except one white have developed quartan malaria. These few observations would indicate a high degree of susceptibility in both races.

This parasite, in various lots of anophelines incubated at 20° C., has required 35 days for the completion of the extrinsic incubation period. The patients successfully inoculated have had incubation periods (intrinsic) varying from 27 to 42 days in duration. This leisurely evolution is an interesting contrast to the other types.

The acute illness observed in negroes has been of relatively short duration as compared to that seen in whites, in whom the course may cover from four to five months. Our cases have all begun with a quartan intermittent paroxysm, which after a month or more may change to a double quartan, but as yet none of our mosquito inoculated patients have exhibited quotidian paroxysms. In general, this disease must be regarded as more severe than tertian, despite the slower evolution. In the latter, the paroxysm covers a shorter period and in the intervals between paroxysms the patient is able to be up and about. In quartan the paroxysm requires more time, and the patient feels inclined to remain in bed on the day following the paroxysm.

Gametocyte production has not been observed until several months after the onset, and is never extensive.

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ENDEMIC TYPHUS OF THE UNITED STATES*

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The term endemic typhus is gradually replacing that of Brill's disease for designating the type of typhus which is endemic in sections of this country. Although endemic typhus of the United States differs epidemiologically, clinically and in its mortality rate from epidemic, or louse-borne, typhus of Europe, it nevertheless is a true typhus. The two diseases are immunologically identical.

Endemic typhus has become an important public health problem in some sections of the country. In a few counties the number of cases outnumber that of typhoid fever. Although the mortality rate is low, the majority of cases are among men of middle age who are incapacitated, as a rule, for four weeks. The case incidence is on the increase, this increased incidence being due not only to more frequent recognition of cases, but to an increase in the actual number of cases. Over 1,400 cases have been reported to date this year.

The members of this Section are primarily interested in endemic typhus from the viewpoint of control. With this view in mind, this discussion will be confined to a brief statement of the facts relative to the epidemiology of the disease, a knowledge which is essential to the establishment of efficient measures of control.

Our knowledge of the epidemiology of endemic typhus is founded upon the work of Brill, Maxcy, Rumreich and Dyer.

In discussing the epidemiology of a disease the rule is to discuss it from the standpoint of geographical distribution, seasonal incidence, age, sex, race, occupation, and so forth, and in somewhat the order given. Since in endemic typhus these various factors are dependent upon the reservoir of the virus and the vector, these will be considered first.

The Vector.—Brill[1] noted the absence of infestation of lice among the cases studied by him. Maxcy,[2] from his studies, found no evidence suggesting louse transmission and sug-

*Read in Section on Public Health, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

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gested that there existed a rodent reservoir of the virus and that the disease was transmitted to man by some blood-sucking insect or arachnid, mentioning fleas, mites and possibly ticks as vectors. The "chigger" or "bedbug" had also been mentioned by some as a possible vector. The question of vector was clarified somewhat by Rumreich,[3] who observed that there occurred in the same general area in which endemic typhus was appearing cases which resembled epidemiologically and clinically Rocky Mountain spotted fever more than endemic typhus. His contention that two distinct diseases were being observed and confused was proven in the laboratory.[4] The fact that there existed two distinct diseases, endemic typhus which is essentially an urban disease, and spotted fever, which is essentially a rural disease and spread by the woodtick, tended to rule out ticks as possible vectors of endemic typhus.

Dyer[5] has repeatedly recovered the virus of endemic typhus from rat fleas which were caught on premises where human cases of the disease had occurred.

Rat fleas are readily infected in the laboratory with the virus of endemic typhus, which virus multiplies enormously in the body of the flea. The virus is also present in the feces of the infected fleas and normal rats have been infected by scratching into the skin such infected feces. Normal rats placed in a cage with rats infected with endemic typhus will remain free from the infection as long as no blood-sucking arthropods are present, but after the addition of rat fleas into the cage the normal rats may become infected.

Although several species of rat fleas have been shown in the laboratory to be capable of transmitting the disease, the seasonal incidence of human cases of endemic typhus corresponds to the seasonal prevalence of the rat flea *Xenopsylla cheopis*.

The bedbug and the tropical rat mite (*Liponyssus bacoti*) have been shown, in the laboratory, to be infectible with the virus of endemic typhus, but neither has been found infected in nature and neither has been incriminated epidemiologically in the spread of the disease to humans. The bedbug is further eliminated as a vector of the virus of endemic typhus by the fact that endemic typhus is a disease of places of occupation and not of domicile.

Reservoir.—Maxcy, from his epidemiological studies, suggested a rodent reservoir of the virus of endemic typhus, possibly the rat or the mouse. Rumreich observed that 78 per cent of the cases of endemic typhus studied by him had had close association with rats. Dyer isolated the virus of endemic typhus from tissues of wild rats caught on the premises where human cases of the disease had been contracted. Mooser had previously isolated a virus of typhus fever from wild rat tissue in Mexico.

From the foregoing epidemiological and laboratory studies the wild rat has been established as a reservoir of the virus of endemic typhus and rat fleas have been indicated as its vector.

With these facts in mind the other phases of the epidemiology of the disease will be considered.

Geographical Distribution.—Endemic typhus of the United States is essentially an urban disease with the greatest incidence in the seaports and having a tendency to spread inland along lines of communication. Cases have, however, been reported which, undoubtedly, have originated on farms.

Seasonal Incidence.—Human cases of endemic typhus may occur at any time during the year, but the greatest incidence is in the late summer and fall.

Occupation.—The disease is more often contracted at places of occupation than at places of residence, particularly among those who are employed at food or grain handling places where rat harborages exist.

Age.—Endemic typhus rarely occurs in children, those of middle age furnishing the greatest number of cases.

Sex.—Males are much more frequently attacked than females. That males are more frequently attacked than females and that the middle age group furnishes the greatest number of cases are undoubtedly due to the fact that endemic typhus is essentially an occupational disease.

Contagiousness.—Case to case transmission has not been noted, although more than one case has originated at the same focus.

The salient facts of the epidemiology of endemic typhus may be summarized as follows:

Endemic typhus is a disease essentially urban, occurring in greatest numbers in coastal cities, in the late summer and fall. The seasonal incidence of human cases corresponds to the greatest prevalence of the rat flea *Xenopsylla cheopis*. The wild rat and its fleas have been shown to harbor the virus in nature. Men are attacked more often than women, with the greatest inci-

dence among the middle age group. It is a disease of places of business rather than of domicile and shows no predilection for any social strata. Case to case transmission has not been noted.

Control.—As the epidemiology of endemic typhus is similar to that of bubonic plague it is believed that plague eradicative measures will also be applicable to the eradication of endemic typhus.

From the standpoint of the individual and his environment there is little to be done in addition to the recognition of the disease and the elimination of vermin.

Recognition of the Disease.—The disease most frequently confused with endemic typhus is Rocky Mountain spotted fever. Since 1930 it has been known that spotted fever occurs in sections of the country other than a few of the Northwestern states and Rumreich has gathered evidence to show that this disease has existed in the East for as long as twenty years. These cases of spotted fever have, in the past, been generally diagnosed as endemic typhus or Brill's disease, and there is apparently still some confusion between the two diseases.

A few of the main differential characteristics of endemic typhus and spotted fever will be outlined.

Epidemiologically, endemic typhus is essentially an urban disease with rat fleas as vectors, while spotted fever is essentially a rural disease with ticks as vectors. A reservoir for the virus of endemic typhus has been shown to be the wild rat, while no reservoir, other than the tick, has been demonstrated for the virus of Rocky Mountain spotted fever. The majority of cases of endemic typhus give histories of close association with rats, while the majority of cases of spotted fever give histories of exposure to tick bites. The seasonal incidence of spotted fever is late spring and summer, while that of endemic typhus is late summer and fall.

With few exceptions, the two diseases can be distinguished clinically, principally by the distribution and characteristics of the lesions. In endemic typhus the lesions are more prominent on the trunk and proximal portions of the extremities and occur rarely on the palms, soles and face. In spotted fever the entire body surface is usually involved with the lesions most numerous on the distal portions of the extremities, especially about the wrists and ankles.

In endemic typhus the lesions are for the most part rose or dull red macules, although maculopapular lesions may develop. In spotted fever the lesions appear as rose or dull red macules, later becoming petechial and pupuric.

The general measures of control are those measures which lead to the destruction of wild rats and their vermin.

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THE RECENT OUTBREAK OF ENCEPHALITIS AT ST. LOUIS*

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Since early in July, 1933, there have been reported in St. Louis and St. Louis County approximately 1,100 cases of encephalitis. This outbreak differed in several respects from the usual encephalitis lethargica, or epidemic encephalitis, as encountered in this country:

(1) The outbreak occurred during the summer and fall of a hot, dry year.

(2) Persons over 50 years of age furnished an unduly large proportion of the cases and especially of the deaths.

(3) Non-fatal cases tended to recover without evidence of mental or physical deterioration.

These peculiarities, together with the clinical picture presented by the cases in this outbreak, suggest relationship to a type of encephalitis of which outbreaks have been repeatedly observed in Japan since 1871. The largest of these outbreaks occurred in 1924 and 1929. Japanese investigators suggest that this ailment represents a distinct entity and have designated it as encephalitis type B to distinguish it from type A, or the usual epidemic encephalitis of Economo.

Epidemiology.—Senior Surgeon J. P. Leake, of the Public Health Service, aided by a corps of trained investigators, has made an intensive epidemiological study of the St. Louis outbreak,

*Read in Section on Neurology and Psychiatry, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

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but time has not permitted detailed analysis of the collected data.

The outbreak had its beginning in St. Louis County and had made considerable headway there before cases were reported from St. Louis proper on about August 18. Earlier cases from the city, however, have been subsequently located. The outbreak reached its peak early in September and then gradually lessened, the incidence for the county where the epidemic began being 230 cases per 100,000 population as compared to 63 for the city. Outbreaks of similar character have been recorded this fall for Independence, Kansas City and St. Joseph, Missouri, and Louisville, Kentucky.

All ages have been attacked, but the 13 per cent of the population above 55 years of age has furnished approximately 35 per cent of the cases and the case fatality rate in this higher age group has been about double that encountered in persons under 55 years of age. Both sexes appear to be about equally susceptible, with perhaps a slight predilection for males among the younger age groups. The limited data available indicate that the incubation period is from 9 to 14 days.

Connected cases and multiple cases in the same household have not been common, being noted perhaps about as frequently as has been usually the case in outbreaks of poliomyelitis.

The method of spread is obscure, although it is felt that milk and water as major factors can be eliminated. The past fall in St. Louis was an especially dry one and streams usually free flowing became stagnant, with a resulting enormous mosquito production. This circumstance naturally suggested the mosquito as a possible vector. Surgeon L. L. Williams, Jr., of the Public Health Service, with a group of assistants, undertook to test this hypothesis experimentally and was soon joined in these attempts by Majors Jas. S. Simmons and V. H. Cornell, of the U. S. Army Medical Corps. As far as I am aware, results to date have been negative.

Clinical Picture.—The clinical picture, largely quoted from Leake, is as follows: clinically, this outbreak has resembled other epidemics of encephalitis, but especially that described as occurring around the Inland Sea of Japan in 1924. It has differed from most other outbreaks in that ophthalmoplegia, ptosis and strabismus are much more uncommon, while demonstrable meningeal involvement is practically uniform in the recognizable cases. As observed thus far, recovery has been more often prompt and complete. The onset is usually fairly sudden, that is, not prolonged over more than 3 days to reach a definite development, with general malaise and a febrile disturbance, often with a headache. Vomiting and other gastro-intestinal symptoms are not uncommon. Evidence of cerebral involvement may be the first indication of the disease. Pronounced somnolence is not the rule; the patients are apathetic, mentally and physically sluggish, stuporous or comatose rather than somnolent; they may be delirious enough to require restraint, but are not noisy. The neck becomes slightly or moderately stiff at some stage in the well developed disease, and the cells in the spinal fluid are above normal in number, rarely exceeding a few hundred, chiefly lymphocytes. The lumbar puncture often relieves the headache permanently. With the fever there is usually a moderate leucocytosis. Some of the chief reflexes and the superficial reflexes, such as the abdominals, are absent and vary from day to day. Actual paralyses occur, but are typically transient. The response of the great toe is dorsal extension on plantar stimulation (Babinski) or on firm downward rubbing of the tibial group of muscles (Oppenheim) in many cases. Bilateral Kernig and Brudzinski are usually present. Tremors are frequent; and the muscles often tend to be somewhat rigid. Constipation and retention of urine are very frequently noted. Difficulty in feeding and the danger of bedsores, as well as the maintenance of isolation, make hospitalization advisable. Painful sensations, as of the abdomen or legs, are not infrequent in the early stages. The fever may last only three days, or it may be prolonged more than two weeks. The symptoms tend to improve with the subsidence of the fever, which is usually by lysis, but not uniformly. A return of the fever usually bespeaks the presence of complications such as cystitis with retention or a bronchopneumonia. The spinal fluid in nearly all of the patients is under increased pressure and is clear. The cell count has been found to vary from 3 to 1300, but is usually from 50 to 350. The cells, as already stated, are usually almost entirely lymphocytes, though polymorphonuclears may be present, even to 50 per cent early in the disease. The sugar ranges from 50 to 80 milligrams and globulin is usually increased. The white blood count has been found to vary from 4,000 to 36,000, but is oftenest between 8,000 and 15,000.

Pathology.—The pathological lesions of the central nervous system consist of perivascular round celled cuffing, diffusely distributed throughout the meninges, brain, bulb and cord without the special localization in the basal ganglia and brain stem noted in epidemic encephalitis. Nerve cell changes ranging from cell swelling to neurophagia are found. Dr. Margaret C. Smith, of Washington University, as reported by Dr. H. A. McCordock, demonstrated inclusion bodies in the kidneys. These bodies were intranuclear and were found in four of seven cases examined up to that time. Hemorrhages in the serous and in the mucous membranes are quite frequently observed.

Experimental Transmission.—Numerous species of animals have been inoculated with material from fatal cases, and Muckenfuss, Armstrong and McCordock reported the establishment of a febrile condition in Rhesus monkeys coming on from 8 to 14 days following inoculation with material from 7 of 15 fatal cases from which attempts were made. The condition has now been carried through 6 generations in monkeys. The central nervous system lesions in monkeys are consistent with those seen in human cases. A number of rabbits and 8 Cebus monkeys were inoculated intracerebrally, but these animals proved refractory, facts which indicate that the investigators were not dealing with a herpes virus. Dr. L. T. Webster, of the Rockefeller Institute for Medical Research, with material supplied him from the St. Louis epidemic, produced a fatal condition in special strains of white mice. Muckenfuss and Armstrong have confirmed this work, using stock strains of mice.

Prevention.—Preventive measures have consisted in the early hospitalization and isolation of cases. The sharpness and extent of the recent outbreak, and its tendency to spread to other cities, suggest potentialities for this disease which can but arouse concern in the minds of the medical profession and the public, and it is to be hoped that every opportunity intensively to investigate this ailment may be fully utilized by those to whom the opportunity may come.

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THE TREATMENT OF PELLAGRA*

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In a clinical talk it is desirable to emphasize the facts of experience rather than theories, however important in themselves. I shall attempt, therefore, to outline the treatment of pellagra under the heads of prevention and of cure.

For prevention we have a remedy simple in itself, but which has proved to be by no means easy of application. This same remedy is useful also and doubtless fundamental in the curative treatment, but again the results plainly declare the need to supplement this remedy. I refer, of course, to diet.

It may be said, then, that the current knowledge of pellagra, if it could be applied, is probably adequate to the prevention of the disease, but is inadequate to its cure in many cases at the time they come under treatment.

That the measures used for the prevention of pellagra and the knowledge necessary for its cure are still grossly inadequate, is illustrated by the following figures: In Mississippi the reported cases showed progressive increase from approximately 6,000 in 1920 to approximately 14,000 in 1929. The reported mortality in Mississippi for 1928 was 1,206 (8.7 per cent).

The reported deaths in North Carolina showed progressive increase from 306 in 1922 to 860 in 1928.

In a series of hospital cases reported in 1931 by Turner from New Orleans, the mortality was 31 per cent "in spite of treatment" (dietary and symptomatic) "along the most approved lines."

I shall now outline the dietary treatment in the words of its chief advocates in their latest publication, Goldberger's article in Tice's Medicine, as revised by Sebrell, and received from the publishers only last week.

"*Preventive.*—The only way to prevent the disease is to see that the individual eats, at all seasons of the year, the foods containing the pellagra-preventive factor. . . . Measures looking to an increase in the supply and ready availability of milk (dairying, cow-ownership) and of fresh meat in localities where the disease prevails are of great practical importance in eradicating the disease. . . . A sufficient quantity of milk and lean meat should be given, together with turnip greens, tomatoes, green peas, spinach and cowpeas. . . . Pure dried yeast is the richest known

*Read in General Clinical Session, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

source of the pellagra-preventive vitamin, and in an emergency or where the proper foods cannot be supplied, its widespread distribution as a temporary expedient is of considerable value.

"*Curative.*—Diet: having clearly grasped that in pellagra, as in beri-beri and scurvy, diet is the primary controlling factor in the production of the disease, the clinician will readily understand that in pellagra, as in these other diseases, a proper diet is itself the specific treatment. With this fundamental principle clearly understood, the attention of the physician will not be readily diverted to the pharmacopeia, which contains nothing of essential importance, so far as this disease is concerned, but will be concentrated upon the feeding. It may be affirmed confidently that success in the treatment of the individual case will be in almost direct proportion to the attention devoted to the proper feeding of the patient.

"The diet outlined for the purpose of prevention will serve satisfactorily in the treatment of the average case. In severe cases, however, some modification is necessary. As in prevention, milk should be the principal article of diet, given in the form that most tempts the appetite of the patient. If the condition of the mouth and the sensitiveness of the stomach are such that only liquid food is practicable, it is advisable to give in addition to milk, beef juices or soups and broths made from fresh meats, in small quantities at frequent intervals, the allowance being increased as the patient recovers the power to digest food. Solid food, particularly fresh lean meat or liver, should be given as soon as the digestive powers of the patient permit, remembering that diarrhea is not in itself a contraindication to full feeding.

"In the average case of pellagra proper correction of the diet is all that is needed. In the severer cases, or where the proper foods cannot be obtained, dried yeast is most valuable in treatment. Pure dried yeast should be given in doses of from one-half to one ounce daily. . . .

"Liver extracts contain enough of the pellagra-preventive vitamin to make them valuable sources of this material, but their expense would appear to limit considerably their practical value. In difficult cases their use in liberal doses may be indicated."

These ideas have been quoted with the purpose not to question but to emphasize their value. And the rest of our discussion is intended not to detract from, but to supplement the advocacy of dietary treatment. I shall refer particularly to two supplementary remedies, sodium thiosulphate and liver, and wish to report one case which I consider illustrates possible advantages to be derived from further investigation of their usefulness.

Mr. A., a white man aged 58, at times was given to the heavy use of alcohol. He was diagnosed to have pellagra in 1921 and was cured. In the fall of 1932 he indulged heavily in alcohol and late in December was admitted to a hospital with classical signs of pellagra again. A note stated that the inside of the mouth was almost one ulcer and so sore that anything, even water, within his mouth caused him great pain. The backs of his hands were peeling off and there were symmetrical lesions on the forearms. He was irrational, delirious, subject to distressing delusions and had to be restrained. Most faithfully and persistently he was given yeast and the proper liquid diet as well as could be under the circumstances, but on January 11 it still looked as if he would die. On that date he was given the first injection of sodium thiosulphate intravenously. Within 48 hours the condition of the mucous membranes of the mouth had so improved that thereafter the problem of feeding was not seriously complicated by this factor. On January 17 the patient asked for his glasses and a paper to read, and on January 18 it was noted that he seemed much better. Between January 11 and 20 seven injections of sodium thiosulphate were given. Along with the improvement of the mucous membranes the skin lesions cleared satisfactorily. On February 7, it was commented that the mouth seemed entirely well, the patient stating that "it is not sore at all."

Nevertheless, though skin and mucous membranes were healed, the following month was anything but a period of satisfactory convalescence. Diarrhea was for a while troublesome, vomiting arose and was persistent, the pulse was alarmingly bad at times, and the mental symptoms occasioned again the resort to the restraining sheet. On February 6 another series of five injections of sodium thiosulphate was begun and on February 8 the diarrhea stopped. Atropine begun on February 23 seemed to bring the vomiting under control. There was no note of irrational behavior after February 25. On March 5 he was able to feed himself and on March 8 it was recorded that he had gained 14 pounds in the past two weeks. On March 9 he complained that his feet burned and ached; on March 10 he sat up and on March 18 was on the outside taking the air in a rolling chair.

The tingling and numbness of the feet became troublesome in May and the fingers became involved in the same symptoms. There was slow and unsatisfactory gain in muscular strength. There was no sign of the blood changes of pernicious anemia. A little liver extract had been given earlier and the patient disliked the taste, so that ventriculin was given, without apparent improvement. Liver extract was again resorted to, and after ten days the patient reported marked improvement. The patient still takes some liver extract because the feet do not feel entirely normal, though the hands are free from symptoms. He seems entirely well.

With reference to the apparent effect of liver in this case, I do not think it suffices to say that liver extracts contain enough of the pellagra-preventive vitamin to make them valuable sources of this material. The patient had for at least three months been getting the vitamin in its natural form as food. This presentation I admit is a narrow basis on which to suggest, especially for cord symptoms, the further trial of liver. It is to be noted, however, that Boggs and Padget considered that the introduction of liver into the diet had been responsible for the reduction in mortality of their hospital cases in Baltimore from 65 to 19.5 per cent.

It is also a narrow basis on which to suggest the further trial of sodium thiosulphate. But it

is to be noted again that Sabry thought his results in 24 cases were much improved by the use of this remedy as compared with his previous experience with dietary measures alone.

I promised to avoid a theoretical discussion. I have previously advanced at considerable length reasons for believing that sulphur deficiency and errors of sulphur metabolism are important in pellagra. This phase of the subject is now somewhat lifted from its theoretical status by the demonstration by Payne and Perlzweig, of Duke University, that in 14 cases of pellagra with extensive dermatitis there was a marked reduction in the cystine content of the finger nails without any appreciable change in the total protein content. With the subsidence of skin symptoms and improvement in the clinical condition, the cystine content returned to normal limits. A low cystine content was not found in 87 others, normal individuals, cases of syphilis and tuberculosis, and pellagrins or recent pellagrins without dermatitis.

The reported uses of sodium thiosulphate, and perhaps of liver extract, are too meager to establish values for these remedies. It does, however, seem to me that both merit further trial.

TREATMENT OF TUBERCULOSIS IN CHILDHOOD*

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Treatment of tuberculosis in childhood presents problems which are quite different from those encountered in treating the adult type of the disease. With children we are usually dealing with individuals who have recently received or are still receiving their first infection, whereas with adults we are usually dealing with individuals who received their infection many years before and who through temporary ill health or sometimes through reinfection are experiencing a lighting up of old lesions. The first problem which confronts us in treating children, therefore, is the location of the source of infection and the removal of the contact between this source and our patient. Location of the source of infection involves careful examination, including x-ray studies of all those who have come in close contact with our patient. This includes parents, aunts, uncles, grandparents, servants, and frequent visitors. It has been appreciated only in recent years that elderly people are often the source of trouble and that the chronic bronchitis from which they suffer may be tuberculous in origin. They do not die of tuberculosis themselves, but they broadcast the disease among their young associates. Some of the most delicate problems in the practice of medicine arise in connection with breaking contact between a baby and an elderly relative or servant who is suspected of being tuberculous. Old people are fond of children and like to kiss them, and my experience has been that parents will do almost anything, even to taking a chance on the disease, rather than insist on breaking the contact and hurting the feelings of the infected person. The extent and severity of childhood tuberculosis depends in good part upon the size, duration and virulence of the dose of infecting organisms as well as the resistance of the host, so that it is essential that the contact be discovered and cut off at the earliest possible time.

Next to breaking contact with the source of infection, rest is the most important therapeutic agent in the treatment of childhood tuberculosis just as it is with the adult form. The decision as to the amount of rest necessary depends upon the evidence of activity of the disease. The most common symptoms of activity of a tuberculous infection are change of disposition and irritability. Also may be present fever, rapid pulse or cough. Complete bed rest is imperative so long as these symptoms last. It may be two or three weeks or it may be several months. The response of children to bed rest is much more rapid than that of adults. As symptoms subside, the patient may be allowed to be up for a little while in the morning and afternoon under close supervision. It is better at this stage of the disease to have no other children around because the sick child wants to do what the well children are doing, becomes unhappy when he cannot do it and is likely to develop an inferiority complex, which takes years to uproot. Each case is different and the physician in charge has to decide upon the amount of activity to be allowed. Unfortunately the little patients will not tell when they are tired and fatigue must be surmised by evidence of irritability. In making such a decision the physician must remember that the prognosis of childhood tuberculosis under ordinary rules of hygienic living is good; infinitely better than the prognosis of the adult form. Therefore, he can allow his patients to be up more quickly and need not subject them to the long periods of rest that

*Read in Section on Pediatrics, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

are necessary for older patients. They should avoid competitive running games for a long time and should not be allowed to play with a group of healthy children, because the desire to follow the leader will stimulate them to unwise exertion. A child playing alone rarely exceeds his strength. He stops when he becomes tired.

Fresh air is essential for the tuberculous just as it is for any growing child. The temperature of play rooms in weather cold enough for artificial heat should be kept between 60 and 70 while the child is playing. At night the room temperature may be disregarded as long as the windows are open. Climate is not considered so important in the treatment of tuberculosis as it once was. Climate is most important, however, in the control of upper respiratory infections, so that if your patient is subject to such infections he will be greatly benefited by a month or two in southern Florida during the winter and spring.

Heliotherapy is helpful to any growing child and probably is particularly good for the tuberculous child. Direct sunshine is better than artificial radiation, possibly because of the air bath that accompanies bathing in direct sunshine or because the sun provides rays that the lamp does not.

The diet should be abundant and simple. It should be particularly plentiful in minerals and vitamins. It is doubtful that anything is gained by giving more calcium than is contained in a quart of milk. The administration of viosterol has not been considered as good as cod liver oil.[1] Orange juice, tomato juice and bananas are particularly helpful. Results with the Sauerbruch-Gerson diet are not conclusive. This diet is base forming, contains low sodium chloride, low carbohydrate, high fat, and vitamins.[2 3]

Tuberculin therapy has not been attended with much success except in phlyctenular conjunctivitis. In this disease, however, results have been remarkably good. It is also beneficial in adenitis.

SUMMARY

(1) The most important point in the treatment of childhood type tuberculosis is to locate the source of infection and cut off contact.

(2) Rest is essential, but good results are obtained without the prolonged rest that is necessary in the adult type of the disease.

(3) Diet, fresh air and heliotherapy are valuable just as they are to any growing child.

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DISCUSSION (*Abstract*)

Dr. W. Ambrose McGee, Richmond, Va.—In the treatment of tuberculosis of childhood we have fewer concrete evidences of improvement in physical signs, the main reliance being placed upon symptomatic improvement. At times it is very difficult to determine whether or not it is advisable to let the little patient out of bed. Recently two very good prognostic aids have been introduced which seem to offer additional and valuable information in ascertaining whether or not the tuberculosis is active. These two aids are the Schilling differential blood count and the sedimentation rate. In a comparative analysis of these two tests and the lymphocyte-monocyte ratio at Blue Ridge Sanatorium (children's division) we recently found in a study of some forty children that in the great majority of instances it was possible to tell from the Schilling count and the sedimentation rate whether or not improvement was taking place. These two tests paralleled the clinical course of the cases where activity was apparent, but in cases of suspicious childhood tuberculosis the Schilling count was more sensitive and accurate. The lymphocyte-monocyte ratio, when studied with an ordinary blood smear stained with Giemsa stain, was not so consistent or informative in its results. The Schilling count caused less fright among children and was more sensitive to slight flare-ups than the sedimentation rate.

Dr. L. J. Moorman, Oklahoma City, Okla.—Dr. Bruce has presented a subject which is hedged about by many difficulties. I should say that to break the contact or control the source of infection is the first step in the treatment of the childhood type of tuberculosis. This is important regardless of the child's condition or the extent of involvement.

Rest should be insisted upon. However, rest in infancy and early childhood is often difficult to secure. Fortunately, this type of tuberculosis tends to heal, even though the results of our efforts only approximate the rest cure as applied in the adult.

The hygienic and environmental conditions must be carefully considered. Adequate feeding is very essential. The food should be adapted to the age and needs of the individual child. Everything possible should be done to promote physical and mental comfort.

Every case is a problem within itself and must have individual consideration. All those who come in contact with tuberculous children are increasingly impressed with the fact that tuberculous infection in infancy is not so serious as we once supposed, and that manifest childhood tuberculosis usually responds to treatment if the therapeutic program is pursued with reasonable intelligence and persistence.

These impressions represent fifteen years' experience in the Oklahoma City Tuberculosis Dispensary, where three or four hundred contact cases are constantly under observation. More than fifteen hundred children have been studied and some of them have been under observation for a period of fifteen years.

ENVIRONMENTAL CASE STUDIES IN THE TEACHING OF PREVENTIVE MEDICINE*

By HENRY E. MELENEY, M.D.,
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One of the most important problems facing the medical profession at the present time is the successful adaptation of medical practice to the rapid advances of medical science and to the changes taking place in the social and economic life of the community. The problem involves, on the one hand, the tendency toward specialization and group practice in medicine; on the other, the growing demand for adequate medical service and health protection for people of all stations in life. Both of these developments tend to emphasize the scientific and impersonal aspects of medicine, and make it easy for the practitioner to forget that the patient is a complete personality with a problem, and that the problem is often one involving not only the patient, but his environment also.

It is important, therefore, that a broad point of view be maintained by the physician in order that he may be of the greatest usefulness to his patients and to the community. The detailed knowledge required before a medical student can obtain his degree may cause his attention to be focussed too narrowly on the finer points of diagnosis and treatment, with the result that he fails to see the picture of the patient as a whole in his natural environment.

Whether a physician is a specialist or a general practitioner his patients constantly represent problems much broader in scope than the mere diagnosis and treatment of an organic disease. The neurotic woman who is often considered an uninteresting case may prove, after thorough study, to be the product of a most interesting environmental problem. Likewise, cases of syphilis and tuberculosis have behind them social and environmental problems of much greater magnitude than are superficially evident in the patients themselves, and even cases of acute infectious diseases like diphtheria and typhoid fever often lead to contact problems of wide scope.

Public health and social agencies have advanced deliberately and extensively into this field of the background of the individual. The education of the medical student, on the other hand, has advanced particularly along the line of scientific diagnosis and treatment. And yet it must still be conceded, as it has been in the past, that the physician is eminently qualified, because of his intimate relationships with his patients, to deal effectively with these background problems as they arise in his daily work. It is the function of the medical school to see that the student is prepared to perform these broader functions of the practitioner.

This is the phase of medicine where treatment and prevention come into closest association. It demands a preventive approach to clinical medicine and a clinical approach to preventive medicine. The preventive approach to the teaching of clinical medicine has received considerable attention in the last few years, but less attention has been paid to teaching preventive medicine from the clinical point of view. The importance of this clinical approach to the teaching of preventive medicine has been emphasized by Leathers,[1] who says:

> "The student should be given the opportunity to grasp the cardinal facts that curative and preventive medicine cannot be divorced from one another and that as a practitioner he (the student) will have responsibilities to his patient and to the community and state which will require the application of the best available knowledge in the prevention as well as in the treatment of disease."

The development of university hospitals and of affiliations between hospitals and university medical schools during the past two decades has provided adequate teaching facilities for dealing with individual patients in the wards and outpatient departments, but these provisions have often left out of consideration the importance of the patient's home and occupational environment in the development of his illness and in its spread to other persons. If the student can appreciate the importance of these environmental factors he will be more likely, when he becomes a practitioner, to study the patient in relation to his environment.

A few medical schools at the present time send their students out into the community under the direction of private practitioners to gain experience in the point of view and problems of private practice.[2] Such work may or may not be a valuable supplement to ward and out-patient study. It places the student in the normal environment of the patient and brings out the problems associated with the home care of the sick, but its clinical value and its application to the prevention of disease depend

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*Read in Section on Medical Education, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

*From the Department of Preventive Medicine and Public Health, Vanderbilt University School of Medicine, Nashville, Tennessee.

mainly upon the attitude of the private practitioner who acts as the instructor. If the student can be given the responsibility of investigating the source of a disease as well as in examining and treating the patient, such work might be developed into an important phase of training in preventive medicine.

At Vanderbilt University the Department of Preventive Medicine and Public Health is stressing the importance of studying the environment and background of patients. In this phase of our teaching two methods are employed. The first method is to hold joint clinics with the Department of Internal Medicine, dealing with cases which are being studied by third-year students in the wards. When a case appears in which an interesting problem in prevention is presented, the student assigned to the case visits the home or place of occupation of the patient with a member of the department, studies the defects in the environment which may have contributed to the development of the disease, and attempts to determine why and how the patient became ill. The results of this investigation are reported to the third and fourth year classes when the case is shown in the weekly clinic in medicine. In this way the whole picture of the disease is presented to a large group of students, and the importance of such investigations in a complete understanding of the case is emphasized.

The second method is an outgrowth of the first. A procedure somewhat similar to ours has already been described by Hiscock[3] as part of the instruction in preventive medicine at Yale University. It is undertaken at Vanderbilt as part of the fourth-year course in preventive medicine and is carried out in cooperation with the Social Service Division and clinics of Vanderbilt Hospital. Cases are used which have been seen in the out-patient department and which have been referred to the Social Service Division of the hospital. When the preliminary investigation has shown that the case is of special interest it is assigned to one of the fourth-year students for further study.

The student first studies the clinical and social service records which have already been obtained and then visits the patient in his home with a social worker. Together they study the environment, contacts, and problems of the patient and determine a course of procedure for the solution of the medical-social problem of the patient and his immediate contacts. Several visits may be necessary in order to gain the confidence of the patient and his family, and to secure all pertinent information on which a program of procedure may be based. Information is secured under the following headings: (a) description of the home environment, including the neighborhood and housing conditions; (b) the family content, including health, education and general intelligence of the individual members of the household together with their attitude toward the patient's illness; (c) the family history as far back as pertinent facts connected with the problem are concerned; (d) the personal history of the patient, including his education, marital history, past and present occupation, suitability of present employment, his personal problems, and his attitude toward his medical-social problem; (e) the social problems of the family, including problems of adjustment to each other and to the environment, and problems of recreation, religion and conflicts with the law; (f) the economic problems of the family, including income, expenditures, financial aid from outside sources, and adequacy of the income for carrying out treatment; (g) the medical problems of the family, including other cases of the disease from which the patient suffers or other diseases entering into the family problem.

With this information in hand, the student prepares a program aimed at solving the problems presented. He follows the patient through any further examinations and through his course of treatment in the out-patient department of the hospital. He arranges for the examination of contacts who may be suffering from the same disease as the patient or from other conditions. This often requires tact and persistence and always requires the establishment of confidence between him and the persons concerned. The student himself follows through the examination of contacts and the establishment of any treatment which is indicated. He makes contact with any social or relief agencies which have dealt with the patient's family, and helps to secure the proper attitude of such agencies toward the case. Where the occupation of the patient is involved the student studies the problem from this angle and suggests remedies which may prevent the recurrence of the disease in the patient or its development in other employees. If there are defects in the habits of the family in regard to environmental or nutritional hygiene the student seeks to remedy these or suggests what remedies should be applied. The immediate and ultimate source of the patient's disease is made an important point of investigation.

When the case has been thoroughly worked up the student prepares a written report to the Department of Preventive Medicine and Public Health and to the Social Service Division of the hospital and presents the case at a seminar of the fourth-year class.

Ten students out of a class of fifty were assigned cases of this kind last year. The diseases studied included tuberculosis, syphilis, nutritional edema, and psychoneurosis. The cases of tuberculosis were both urban and rural. One of them demonstrated the transmission of the disease through four generations. Another emphasized the difficulty of home care with inadequate facilities and lack of income. In the families of two tuberculous patients cases of syphilis were encountered which had married while under treatment for the disease. A case of congenital syphilis revealed a tragic problem involving syphilis in both parents, failure of support, conflicts with the law and contacts with relief organizations. In a case of nutritional edema the ignorance of the mother and inadequate wages were shown to be important factors in the development of the disease. A case of psychoneurosis which first presented the symptoms of gastric ulcer brought up the problem of attempts at suicide and maladjustment to an apparently normal rural environment.

The students used their own initiative in working up these cases. They did it in their free time without interfering with their other medical studies. They entered into the work with enthusiasm and their reports indicated thoroughness in their investigations and appreciation of the opportunity to see these cases from the broadest point of view. They frequently gave unsolicited expression to the feeling that this type of study had given them a different conception of the problems of medical practice than they had obtained from hospital and out-patient work. It is necessary, of course, that this type of instruction be carefully planned and supervised. It requires an efficient and interested corps of social workers in connection with the hospital. The cases must be carefully selected. The students must have opportunity for frequent conference in working out the problems presented, but at the same time they must feel a responsibility for carrying through the study on their own initiative. With an adequate staff of social workers, a well-organized department of preventive medicine, and a proper spirit of cooperation, some such program could probably be developed to advantage in most medical schools.

In summary, it seems clear that some procedure is needed to impress upon medical students the importance of the clinical approach to the practice of preventive medicine and to emphasize the importance of environmental factors in the development of disease. If some such experience as I have outlined could be furnished to all students in medicine, they should develop a point of view which would make their work more effective in solving the medical and social problems which they will face in the practice of their profession.

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DISCUSSION (*Abstract*)

Dr. W. S. Leathers, Nashville, Tenn.—The paper by Dr. Meleney is of importance because it emphasizes particularly the value of environmental factors in causing illness and the need for a more careful study by medical students of patients with reference to the social and economic conditions which may effect recovery. We have endeavored in planning the course of instruction for medical students to include phases of work which appear to us of value in affording students a better conception of the responsibility which they should assume in the application of preventive measures in general practice. We have endeavored to guide students in a study of preventive medicine and public health so as to show the relation between the prevention and cure of disease. Each medical school must determine what factors are desirable in developing this phase of teaching. It may be that in some centers opportunities are afforded which would not exist in others. I am, however, convinced that it is possible to establish in a medical school a well rounded and stimulating course of instruction in preventive medicine and public health. It is certainly not sufficient to leave this responsibility to the faculty as a whole. This will not prove successful. There is need for a department of preventive medicine and public health which assumes responsibility for teaching and the correlation of departmental activities so as to stimulate interest in this phase of medical service and to develop an interest in investigative work concerning problems which rightfully belong to the field of public health.

The use of preventive measures in practice is being increasingly emphasized. The future practitioner should and must assume a larger responsibility in the application of the preventive aspects of medicine. The use of the case study method in teaching students has proven stimulating and helpful in our work. It is possible to carry out a number of studies which enable the students to demonstrate the integration of preventive and curative medicine. Dr. Meleney has described in detail the plan which is used at Vanderbilt in this respect. Obviously it is not possible to use this method unless there is teaching personnel to give general supervision.

Dr. Russell H. Oppenheimer, Atlanta, Ga.—The subject which was presented by Dr. Meleney was brought out also at the meeting of the Association of American Medical Colleges at Minneapolis this past November. As was pointed out by one of the discussants, we all use environmental studies in the diagnosis and treatment of patients. Environment is one of the things which go to make up what we term the personality of the patient. Our recent broader viewpoint has taught us that both physical and mental health are greatly dependent upon the patient's experiences in life and his reaction to them. Thus, we may find in environment not only the source of infection in one instance but in others the situation which induces or precipitates illness. Therefore, occupation, individual and family habits of life, religious, family and financial conflicts, may both bring about disturbances of health and (if not withdrawn) preclude successful treatment. Consequently, it has become necessary in diagnosis and treatment to consider the patient as he finds himself in his own complex situation in life. Of course, those who have well developed departments of preventive medicine and well developed departments of social service are at a distinct advantage in their ability to carry out environmental case studies both in prevention and treatment. We should all look forward to the development of such departments, but having done so we will still need to consider the patient from the fuller viewpoint of a social individual.

THE ARREST OF NUTRITIONAL CATARACT IN THE ALBINO RAT BY THE USE OF VITAMIN G (B_2)*

By WILLIAM C. LANGSTON, M.D.,
and
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In 1931, Day, Langston and O'Brien[1] demonstrated that by withdrawing vitamin G from an otherwise normal diet, cataract was manifested in young albino rats in 35 out of 37 cases (94 per cent) in from 60 to 87 days. O'Brien[2] in December, 1932, reported similar findings, using albino and hooded rats. In his series, the cataracts appeared by the eighty-fourth day. He also stated that the addition of vitamin G to the experimental diet caused immediate arrest of cataracts developed under the deficiency. In February, 1933, Langston and Day,[3] using the wild gray rat (*Mus norvegicus*) under the same dietary regime, reported the appearance of cataracts in 29 of 34 cases (85 per cent) at an average of 72 days. The same authors,[4] using various deficient diets with the albino rat, obtained similar results. On one of these diets containing 25 per cent whole wheat, and hence a small amount of vitamin G, cataract developed, but at a later date. Yudkin,[5] in September, 1933, reported the development of cataract in a series of 12 young albino rats fed on a vitamin G deficient diet. He reported also a second series of animals which had been stunted for 60 days by supplying them small amounts of yeast before they were placed on a wholly deficient diet. These animals failed to show cataracts after 12 weeks on the deficient diet. He reported one case in which the missing vitamin was promptly supplied when the lens opacity was first noted, with the result that all signs of cataract had disappeared after 3 weeks. Langston, Day and Cosgrove[6] repeated the experiment, using albino mice, and observed cataracts in 45 of 47 cases (96 per cent), the average time of appearance being 48 days. The shorter time of appearance of opacities in the mice was probably due more to improved methods of observation and experience than to any specific differences as compared to the rats. The same authors[7] have obtained similar results with four strains of chicks, and in at least one case with the monkey (*Macacus rhesus*).

While this paper does not deal directly with the production of cataract under a vitamin G deficiency regime, but rather with the arrest of this condition, it might be well to give a brief summary of our work on the former phase of the problem.

In our laboratories, and including only the albino rats and mice and the wild gray rats, there were 118 animals which lived up to the minimum time of appearance of cataract for the respective species. Of these, 109, or 92.4 per cent, exhibited cataract. The majority of these were observed ophthalmoscopically and were checked by histopathologic sections.

In all three series of animals the same diet was used. Young healthy animals at weaning age, and free from any manifestations of congenital cataract, were given unlimited amounts of a modification of Sherman and Spohn's[8] vitamin B complex deficient diet and distilled water. In order to minimize the possible access to vitamin G in the excreta (Page[9] and others), they were placed in metal cages with raised screen floors. Adequate controls were used.

The diet (No. 625) had the following com-

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*Read in Section on Ophthalmology and Otolaryngology, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

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*Great assistance was rendered by Dr. K. W. Cosgrove, of Little Rock, in the ophthalmoscopic examination of the animals. Mr. William Darby gave valuable technical assistance.

position: casein (freed from water-soluble vitamins by treatment with 60 per cent alcohol), 18 per cent; Osborne and Mendel's salt mixture, 4 per cent; cod liver oil,* 2 per cent; butter fat, 8 per cent; corn starch, on which had been evaporated an 80 per cent alcoholic extract of rice polish, 68 per cent.

The general deficiency manifestations were noted in previous reports (cited above) and in appended references. These consisted largely in those lesions encountered in the so-called "rat pellagra" syndrome. After an early slight increase in weight there was eventually an actual loss, but the terminal weight usually exceeded the weight at the beginning of the feeding period. Alopecia was usually encountered in the white and gray rats, but was less frequently seen in the mice. Cutaneous ulceration, salivation and stomatitis with labial crusting, slight hemorrhages of the mouth, nostrils and anus, mild diarrhea and priapism were other observed manifestations. There were no nervous manifestations exhibited.

Vaginal smears made on a number of females indicated that sexual development was retarded, but the power of reproduction was not destroyed, since some animals which had reached mature cataract were returned to normal diet and subsequently produced normal young. Incidentally, these young showed no signs of congenital cataract.[7]

Increased lacrimation was usually noted, followed by an edema and reddening of the conjunctiva and margins of the lids, accompanied, or followed, by discharge and encrustations of the lids which sometimes sealed them. It was usually during this acute stage that mature cataract became evident, but such a condition was sometimes encountered in a "dry" eye. Cultures from the eyes of affected animals revealed nothing significant, and pus from affected eyes caused no conjunctivitis in the eyes of normal rats into which it had been placed. For these reasons, it can reasonably be assumed that infection played no part in the etiology of the observed lens changes. The ophthalmoscope revealed that, previous to this "acute" stage, there was seen an anterior interstitial keratitis with, or without, vascularity of the cornea. In most cases, this keratitis proved to be transient and disappeared after varying intervals of time. Histologically there was noted some proliferation and keratinization of the anterior corneal epithelium and an occasional microscopic corneal ulcer.

In our series of 118 animals, cataract became manifest in from 35 to 87 days. As viewed through the ophthalmoscope, this first appeared as an irregularity of refraction seen as sectors of light and shadow which subsequent sections suggested as having been due to separation of the lens fibers. Later there could be seen spicules, or striae, and in some cases ring-like opacities. If allowed to continue on the deficient diet the cataracts progressed to maturity.

The histopathologic picture varied with the degree of maturity of the cataracts. The lens changes were, as a rule, very rapid and progressed at a greater rate during the acute stage of the general eye condition. Usually the cataracts developed similarly and simultaneously in the two eyes of a rat. At other times, cataracts developed on one side before any changes were apparent in the opposite lens. In one case, after the development of a mature cataract on one side, the animal was given a source of vitamin G in the diet and the opposite lens remained normal for several months—until the animal was killed for sections. The type of cataract was usually the same for both sides, but occasionally it appeared nuclear on one side and cortical on the other. In our experience the opacities appeared more frequently in the cortex.

The earliest changes noted in the histopathologic sections were those of proliferation of the lens epithelium and a separation of the lens fibers. The spaces so formed were usually filled with coagulated fluid. In some areas the lens fibers contained small round vacuoles filled with coagulum. Others showed fine granular degeneration. Morgagnian globules were frequently seen. In later stages massive destruction of lens fibers occurred, leaving large, granular, amorphous masses of lens debris. In some sections more than half of the lens seemed to have undergone degenerative changes. The ciliary body, iris and retina apparently were not affected.

EXPERIMENTAL WORK

Since we had found that, for several species, cataract resulted from G-avitaminosis in a large percentage of cases, and also that such experimental cataract could be prevented by the inclusion of an adequate amount of vitamin G in the diet, we determined to direct our investigations toward other phases of the problem. With incipient cataract induced under avitaminosis,

*The cod liver oil used in the diet of this experiment was supplied by The E. L. Patch Company, Boston.

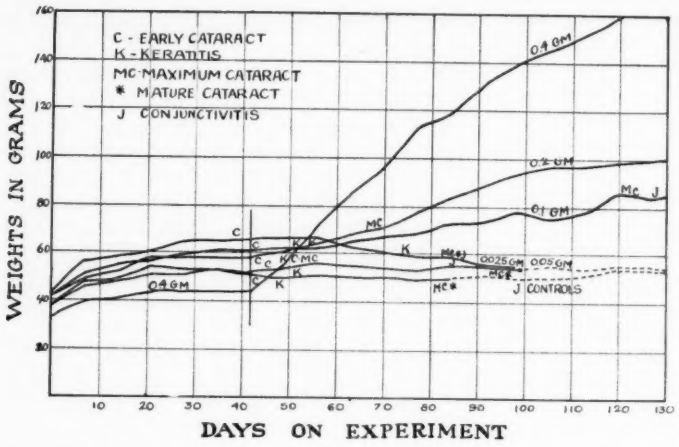

Fig. 1

Average growth curves of albino rats given a vitamin G-deficient diet, supplemented after the forty-second day by graduated amounts of skim milk powder. The time of appearance and arrest of cataract and other ocular manifestations is indicated on the curves.

would the addition of vitamin G to the diet of the animals have any effect upon the progress of cataract development, and if so, in what quantities must the vitamin be added for maximum effect? Would the addition of the vitamin G-containing food have any corrective effect upon cataracts already formed, that is, could a "cure" be effected?

In an attempt to answer these questions a series of 29 young albino rats of about 21 days of age and weighing 30 to 40 grams was placed on the same vitamin G deficient diet used in the preceding experiments (diet 625) for a period of 42 days. Previous experience had indicated this to be about the time needed for depletion of stored vitamin and, in many cases, to induce early lens changes. Thus, some of the animals at this stage of the experiment showed a clear lens and cornea, while others showed early corneal and lens changes, and all of them were presumably depleted of their natural store of vitamin G. They were then fed on diet 625 supplemented by graduated amounts of a vitamin G-containing food in the form of skim milk powder in daily amounts as follows: 2 animals on 0.4 gram; 8 on 0.2 gram; 10 on 0.1 gram; 2 on 0.05 gram and one on 0.025 gram. The remaining 6 animals were continued on the deficient diet without the addition of any vitamin G and were used as negative controls.

All animals were subjected to daily inspection and to weekly ophthalmoscopic examination. At death the eyes from most of the animals were sectioned and examined histopathologically.

In order to be able to correlate and tabulate the findings, the conventional signs of 1 plus to 4 plus were used, 1 plus indicating early lens changes of incipient cataract and 4 plus fully developed, mature cataract, with 2 and 3 plus intermediate stages. Averages were computed for the number of days on the experiment required to produce: first, keratitis; second, early lens changes; third, maximum cataract development (whether mature or not); fourth, mature cataract; and fifth, conjunctivitis. These figures and weight curves, based on weekly weight records, are given in the chart (*Fig. 1*).

RESULTS

The results obtained (*Table 1*) naturally fall into two main categories: one in which the cataract development was arrested before reaching maturity, and the other in which maturity was reached, but some retardation was noted; in other words, an arrested and a non-arrested group.

The first category includes the animals receiving 0.4, 0.2 and 0.1 gram per day, respectively. In this group of 20 animals, complete arrest of cataract development was effected in 15 (75 per cent), while in the remaining 5 the cataracts went on to maturity. Of the animals receiving 0.4 gram per day, neither went to maturity and the development of cataract was arrested within an average of 10 days. One of these two rats (No. 1714) exhibited a 2 plus cataract when placed on the milk powder (forty-second day) and after 242 days showed no further progress toward maturity. On the two hundred and forty-second day after receiving the milk powder, it showed a clear ring of new lens substance surrounding the older cataractous portion. The other (No. 1710) showed a clear lens when placed on the milk powder, a 1 plus on the sixty-third day and no further development after that time until it died on the two hundred and eighteenth day.

Of the 8 rats receiving 0.2 gram of skim milk per day, 6 exhibited arrested cataract by the

sixty-eighth day (average), or 26 days after receiving the vitamin. One of the remaining two animals (No. 1745) showed a 2 plus cataract when placed on the milk powder and rapidly progressed to maturity on the forty-fourth day. The other (No. 1741) showed a 1 plus lens when placed on the milk, yet progressed definitely and rapidly to maturity by the seventy-second day. No explanation is offered for this apparent exception unless it was due to the fact that this particular animal had a higher vitamin G requirement than the average for its species. Two rats of this group (Nos. 1713 and 1740) also showed cortical rings of new lens substance (*Fig. 2*).

The 10 rats receiving daily amounts of 0.1

Table 1

COMPARATIVE PERIODS IN WHICH OCULAR MANIFESTATIONS OF VITAMIN G DEFICIENCY WERE ARRESTED FOLLOWING ADMINISTRATION OF THE VITAMIN IN THE FORM OF SKIM MILK POWDER(a)

Rat No.	Milk powd. (gm.)	Keratitis (days)	Early Cataract (days)	Eyes on 42nd day	Maximum Cataract		Mature Cataract (days)	Conjunctivitis (days)
					Days	Degree		
1710	0.4	42	63	Clear	63	1+	*	**
1714	0.4	58	42	2+	42	2+	*	**
Average		50	52		52			
1713	0.2	30	42	K	63	3+	*	**
1737	0.2	58	51	Clear	113	3+	*	**
1738	0.2	51	44	1+	58	3+	*	**
1740	0.2	37	51	K	72	2+	*	**
1741	0.2	58	42	1+	72	4+	72	**
1742	0.2	79	44	Clear	86	2+	*	**
1744	0.2	65	37	1+	37	1+	*	**
1745	0.2	37	37	2+	44	4+	44	**
Average		52	44		68		58	
1717	0.1	32	31	1+	94	4+	94	94
1720	0.1	44	44	Clear	67	4+	67	58
1721	0.1	81	32	1+	94	2+	*	**
1727	0.1	65	32	Clear	135	2+	*	171
1728	0.1	37	49	K	135	2+	*	**
1746	0.1	56	35	1+	120	4+	120	167
1747	0.1	70	49	Clear	167	3+	*	**
1748	0.1	70	56	Clear	167	3+	*	**
1749	0.1	35	43	K	133	2+	*	148
1751	0.1	36	43	1+	106	2+	*	**
Average		53	42		122		94	127
1718	0.05	44	51	Clear	74	4+	74	58
1730	0.05	60	42	1+	114	4+	114	114
Average		52	46		94		94	86
1719	0.025	74	39	1+	87	4+	87	87
1711	none	49	42	1+	86	4+	86	77
1715	none	42	50	K	113	4+	113	142
1716	none	67	58	Clear	94	4+	94	94
1729	none	31	37	1+	58	4+	58	79
1743	none	44	37	1+	58	4+	58	65
1750	none	49	35	1+	84	4+	84	133
Average		47	43		82		82	98

(a) The tabulated number of days date from the time the rats were placed on the deficient diet. The feeding of milk powder supplements was started on the forty-second day.

K Keratitis, but no cataract.

* Did not reach maturity.

** No conjunctivitis manifested.

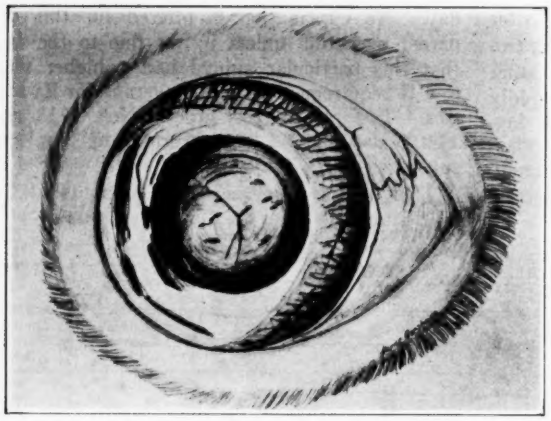

Fig. 2
An artist's drawing of the eye of an albino rat, showing cataract and new lens tissue as viewed through the ophthalmoscope. The shaded portions indicate the cataractous areas of the lens.

gram of milk powder exhibited arrest of cataract in 7 and mature cataract in 3. The arrest had been effected at an average of 122 days, or 80 days after receiving the vitamin G. The degree of development in this group was slightly greater than that in the group receiving 0.2 gram. In other words, it took a longer time to arrest the developing cataract on 0.1 gram than it did on 0.2 gram and the cataracts made slightly greater progress toward maturity on the lesser amount of the vitamin G-containing food. The three remaining rats of the group exhibited mature cataract on the sixty-seventh, ninety-fourth and one hundred twentieth days, respectively.

In the two animals on 0.05 gram of milk powder, cataract developed to maturity on the seventy-fourth and one hundred fourteenth days, respectively. The single animal receiving 0.025 gram per day showed mature cataract on the eighty-seventh day.

All of the negative controls, which received no milk powder at any time on the experiment, exhibited mature cataract at an average of 82 days.

In addition to the lens changes described above, all of the animals under observation evidenced keratitis at some time during the experiment. At times, it occurred before the earliest lens changes were noted and in other animals it appeared at a later date. Vascularity of the cornea was frequently observed and the vessels often became atrophic and obliterated even while the animal was on a wholly deficient diet. The keratitis often disappeared early and in some cases reappeared subsequently.

None of the animals receiving 0.2 gram of milk powder, or more, developed conjunctivitis and five of those on 0.1 gram did not show this condition. All other animals of the series, including the controls, did show some inflammation of the conjunctiva and lid margins. The conjunctivitis was seen at a later date in those animals which received the milk powder.

In no case of the series did we observe any evidence of repair of damaged lens substance following the administration of vitamin G in any form. As indicated above, three of the animals (Nos. 1713 and 1740 on 0.2 gram and No. 1714 on 0.4 gram) exhibited rings of new lens substance surrounding the older cataractous portion of this structure. This probably would have occurred in other animals had they been kept on an adequate diet for a sufficient period of time. This would indicate that, although the destroyed lens fibers were not repaired, the power of lens proliferation was not destroyed. This is not surprising when it is recalled that, following the addition of vitamin G to the diet, general body growth was resumed (the weights being approximately trebled) and the lens takes part in this general body growth.

In addition to the animals tested on milk powder, other series were run on other vitamin G-containing foods such as yeast, autoclaved yeast, whole wheat, and wheat middlings. Since comparable results were obtained in all, it is assumed that the results obtained and described for skim milk powder were not due to any peculiarity of skim milk *per se*, but to some substance contained in all of the food substances mentioned, namely, vitamin G, the relatively heat-stable factor of the vitamin B complex.

DISCUSSION AND CONCLUSIONS

Fig. 1 shows the composite weight curves of the several groups of animals on the respective amounts of milk powder and the composite points (days on the experiment) on these curves at which the respective pathological manifestations had become apparent. It will be noted that the increase in weight of the animals was in direct proportion to the amount of vitamin G-containing food received and that the time

of appearance of maximum cataract development was roughly in inverse proportion to the amount of vitamin G obtained, being 10, 26 and 80 days after the administration of vitamin G in amounts of 0.4, 0.2 and 0.1 gram of skim milk powder, respectively. This would seem to indicate that the cataract-preventive and the growth-promoting factors are identical.

At the same time, it will be noted that skim milk powder in amounts of 0.05 gram or less was not sufficient to prevent maturity of the cataracts, but appeared sufficient to effect a retarding influence, as can be seen by comparing the time of appearance of maximum cataract in these animals with that of the controls. Of course, in these cases, the maximum time of appearance also represented the time of maturity, since the cataracts in all of the animals on 0.05 gram or less developed to maturity.

Conjunctivitis appeared in 5 animals receiving 0.1 gram at an average of 127 days; in both animals on 0.05 gram in 86 days; and in all 6 controls at an average of 98 days. No conjunctivitis was noted in animals receiving 0.4 or 0.2 gram per day.

From these observations, it may reasonably be concluded: first, that in a majority of cases, milk powder in amounts of 0.1 gram or more per rat per day was sufficient to arrest the development of cataract in from 10 to 80 days, the time required being in inverse proportion to the amount of milk powder supplied; second, that milk powder in amounts of 0.05 gram or less per day was sufficient to retard the appearance of mature cataract, but not sufficient to effect complete arrest, the degree of retardation being in proportion to the amount of milk powder supplied; third, that 0.1 gram or more was sufficient, in most cases, to prevent the appearance of general ophthalmia and that this condition appeared in all animals receiving less than 0.1 gram per day; fourth, that keratitis was seen in all animals regardless of the amount of milk powder supplied; fifth, that no curative effect of the milk powder was noted, but that new lens substance was laid down in the cortical areas of cataractous lenses following the administration of vitamin G in some cases where the animals were kept for a sufficiently long period.

SUMMARY

A brief résumé of the production of cataract in rats and mice on a vitamin G-deficient diet is given.

A series of 29 young albino rats was kept on a vitamin G-deficient diet for 42 days, at the end of which time they were depleted of their store of vitamin, and in most cases had developed incipient cataract. The animals were then given graduated amounts of a vitamin G-containing food in the form of milk powder, in amounts of 0.4, 0.2, 0.1, 0.05 and 0.025 gram per rat per day, respectively, in addition to the basal diet. Adequate controls were used. Amounts of 0.1 gram or more per day proved sufficient to prevent the maturing of cataracts in 75 per cent of the cases. Amounts of 0.05 gram or less per day were sufficient to retard the development of the cataracts, but not to prevent their maturing. The effect of vitamin G thus supplied was in direct proportion to the amount given.

No curative effect of the vitamin was noted, although new lens substance was laid down in some animals which were kept for longer periods of time. Amounts of 0.1 gram or more per day were sufficient to prevent the appearance of general ophthalmia. All animals on the experiment, including the negative controls, manifested keratitis.

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DISCUSSION (*Abstract*)

Dr. K. W. Cosgrove, Little Rock, Ark.—It has been conclusively shown that cataracts will develop in animals given a diet lacking only vitamin G (B_2). It has also been shown by the data presented here today that these experimental cataracts may be arrested by the addition of vitamin G to the diet.

It should be the purpose of those engaged in animal research in the field of medicine to show, if possible, a relationship between pathological conditions produced in animals and known pathology in human beings. The question as to whether or not vitamin G deficiency is responsible for some forms of human cataract is difficult to answer. The difficulty in determining when a human cataract is arrested and, also,

the minimal requirement of vitamin G for each individual, makes the problem more difficult. As previously reported in discussion of Dr. Yudkin's paper at the American Medical Association meeting this year, a survey of fifty private patients, who had been carefully questioned regarding their diet, showed that 64 per cent were taking only very small amounts of food rich in vitamin G. This proved nothing, but did suggest a possible connection between vitamin G insufficiency and some cases of human cataract.

In an attempt to bring more light upon this question, careful histories of sixty-one inmates of a home for the aged were taken. The patients were questioned regarding their vision, especially any recent changes, and regarding their diet and any recent modifications. Their use of foods rich in vitamin G, such as milk, greens and lean meat, was taken as a measure of their vitamin G intake. To prevent prejudice from entering into the investigation, the patients' answers were recorded verbatim by Miss Compere, of the Baptist State Hospital (to whom I owe a great deal for her assistance). The patients were then examined and records were made of the type and degree of lenticular opacities, if any were present. Results were compiled and are as follows: the average age was seventy-nine. Twenty-one of the sixty-one showed no signs of opacity in either lens. Eighteen of these normal cases had been accustomed to eating daily at least two of the foods just mentioned. The other three had been taking large quantities of one of them (milk).

Of the forty cases showing lenticular changes, twenty-five had cortical opacities in one or both lenses. Fifteen had nuclear opacities. Only one eye of one patient showed a mature cataract. The twenty-five cases of cortical cataract were divided by the histories into eight which were progressing rapidly, eleven which were apparently arrested, and six in which arrest was questionable. The eight cases with a history of rapid loss of vision had not for several years eaten any food rich in vitamin G. The eleven with cataract apparently arrested had added to their diet since coming to the home milk or buttermilk. The six questionable cases were eating small amounts of some food rich in vitamin G.

The nuclear cataracts were all progressing slowly, according to the patients' histories. Eleven of these patients were eating large amounts of vitamin G. Four were eating moderate amounts.

Although this series is small and no definite conclusions are justified, several of the findings are suggestive of a direct relationship between vitamin G intake and the arrest of development of cortical opacity of the lens. There was in this series apparently no relationship between the diet and the progress of opacity occurring in the nucleus of the lens. The fact that twenty-one cases showed no cataract, although they had reached the cataract age, and had been eating large amounts of vitamin G, suggests a relationship between the vitamin G intake and the occurrence of cataract. In order to establish a definite relationship between vitamin G shortage and senile cataract, it will have to be shown in thousands of cases and over long periods that the addition of food rich in vitamin G to the diet will arrest cortical opacities of the lens. The diet that has been used by my private patients consists of: milk three times a day, liver three times a week, and frequent use of green vegetables and some lean meat. On this diet six cases have been arrested for more than a year, and one case went on to maturity in one eye.

It is apparent that this data has not proven any theory regarding the etiology of senile cataract. It does suggest a method whereby it should be possible for ophthalmologists, especially of the South, where cataract is more prevalent, ultimately to prove or disprove a relationship between vitamin G and so-called senile cataract.

Dr. J. N. McLane, Pensacola, Fla.—It is certainly up to us as ophthalmologists to regulate the diet of the patient with an early cataract. In this way we can prove the relation of vitamin G to cataract formation in man.

At present when a patient consults us with a beginning opacity of the lens we are unable to offer him any relief until the cataract has matured.

Dr. Langston (closing).—While we do not know what clinical bearing, if any, these results may have, we feel that they suggest a possible etiological factor in some cases of senile cataract. It would be contrary to previous scientific experience if this were not true. The cataracts obtained in our animals appeared with remarkable frequency, showing a high incidence in rats, mice and chicks. If this experimental condition in these animals is not analogous to clinical cataract, the human would prove itself to be quite the exception in this particular. The readiness with which the cataracts were arrested by the addition of the vitamin to the diet suggests, at least, that the addition of foods rich in vitamin G to the diet of patients showing incipient cataract might prove beneficial, at least in some cases. Unless otherwise contraindicated, it could do them no harm. If careful dietary histories were taken on all cases of early senile cataract and, in those cases where there was apparent some vitamin G deficiency, the missing vitamin were promptly and adequately supplied, the results obtained should indicate whether the experimental cataracts obtained by us are or are not analogous to clinical cataract.

ECLAMPSIA: REPORT OF A CASE*

By M. Pierce Rucker, M.D.,
Richmond, Va.

Mrs. F. is an ideal patient, in that she cooperates perfectly. Only once in the two and half years that I have had her under observation has she failed to follow directions, and that was when her mother was ill and needed her care. I first saw her on February 28, 1931. Her physician, Dr. Murray, sent her into the Johnston-Willis Hospital on account of severe toxemia. At that time she was 25 years old. In 1928 she had an abortion at three months. Otherwise her past history was negative. Her family history is unimportant. According to Naegele's rule her date of confinement

*Read in General Clinical Session, Southern Medical Association, Twenty-Seventh Annual Meeting, Richmond, Virginia, November 14-17, 1933.

should have been April 17, 6 weeks after she entered the hospital.

Two weeks before entering the hospital the patient began to have severe headaches and swelling of the face, hands and feet. She had three attacks of visual disturbance, black spots before the eyes. The first occurred a month before her admission to the hospital and the last a week before that time. Since the last spell she had not been able to see well.

Her blood pressure on admission was 212/120 mm. of mercury. The urine solidified on boiling and contained a number of granular casts. Her vision was so poor that she was unable to count fingers. The patient was put to bed on a diet of cream of tartar lemonade. The next day her condition was practically unchanged and it was decided that labor should be induced. Accordingly she was given an ounce of castor oil and a large catheter was introduced into the uterus. Twenty-four hours later I delivered her of a stillborn male child, by breech extraction, under tribromethyl alcohol (avertin) anesthesia. The baby weighed 4¼ pounds and measured 17 inches in length. Postdelivery care consisted of cream of tartar lemonade and sodium bromide and chloral hydrate at bedtime. On March 3 she was allowed tea and toast. At 6:00 a. m., March 4, the patient had a typical convulsion. She was given 20 c. c. of a 10 per cent magnesium sulphate solution intravenously at once and soon afterwards two drams of tincture of digitalis. The digitalis was repeated twice in dram doses. Her blood pressure was 210/110.

On March 5, it was noted that the patient felt better, but was restless. She was given 2 c. c. of 50 per cent magnesium sulphate intramuscularly. At 4:00 p. m. she had a second convulsion. Twenty c. c. of a 10 per cent solution of magnesium sulphate was given intravenously. At bedtime she was given 2 drams of paraldehyde. Recovery from this time on was uneventful. On March 7 a low protein diet was allowed. It was noted that her eye grounds showed a blurring of the discs. Her blood pressure was 190/120. On March 10 she was allowed to sit up and was discharged the next day. Her temperature was normal throughout the puerperium.

On March 31 Dr. Murray wrote that her urine had cleared up.

The patient returned for her postpartum examination on April 11, 1931. She was having constant headache and her vision was so poor that she could not read news print. The blood pressure was 135/90. The urine was negative. The uterus was retroverted.

On June 8, I have a note that her vision has improved. She has been menstruating regularly since April. Her uterus is still retroverted and her blood pressure is 170/105.

On July 6, the patient complained of being nervous. The position of the uterus was corrected and a No. 2 Smith pessary fitted. Her blood pressure was 130/90. In October the uterus was found to be in good position and the pessary was removed. The blood pressure then was 140/90.

On December 23, her blood pressure was 148/95. There were a few cysts in the cervix and these were treated with a cautery. In January, 1932, the blood pressure was 135/85. The uterus was again retroverted.

The patient came back on October 26 complaining that she had gone over her period a few days. The uterus was anteflexed and firm and I did not think at the time that she was pregnant. Her blood pressure was 135/70. By the end of November she had begun to be nauseated and it was evident that I was mistaken. Her blood pressure then was 125/70 and the urine was free from albumin. The patient was very anxious for a child, and it was agreed to let the pregnancy continue until the first sign of kidney involvement. On December 22, she was complaining of headache and there was a trace of albumin in the urine. Her blood pressure was 140/85. This was the time that the patient was engaged in home nursing. She was put upon 18 hours a day bed rest and a meat-free diet. On December 29, the specific gravity of the urine was 1.012 and it was free from albumin. The blood pressure was 130/70. From this time on, her pregnancy was uneventful except for a cold in March and a crop of boils in April. The systolic blood pressure ranged from 120 to 135. The urine remained free from albumin with a varying specific gravity.

On June 6, the blood pressure was found to be 150/105, and the urine showed a trace of albumin. The patient had had one blind spell, but no headache. She was sent into the hospital and labor was induced with castor oil (oz. 1), quinine (gr. 5), and rupture of the membranes. The child, a female, was delivered with low forceps three hours and forty-eight minutes after the membranes were ruptured. The anesthesia consisted of a barbiturate (sodium amytal) and hyoscine with a little ether for the forceps operation. The baby weighed seven and a quarter pounds and did well. The puerperium was normal.

Postpartum examination on July 6 showed a blood pressure of 135/95 and a small anteflexed uterus.

DISCUSSION

The first point of interest in this case is the treatment of the eclampsia. Her convulsions were easily controlled with magnesium sulphate and the patient had not the prolonged coma that makes the nursing care of these patients arduous. Nothing in my experience has so simplified the treatment of eclampsia as the intravenous use of magnesium sulphate. In only two cases have I been unable to control the convulsions with one or two intravenous injections. I have never used more than three injections. Not only are the convulsions controlled but there is rarely any coma afterwards. This makes looking after the patient much easier. The patient should have rest. I do not believe that enough emphasis has been placed upon rest. These patients are just as ill as if they had pneumonia or typhoid fever, and they need rest just as much. For that reason I am opposed to gastric lavage and colonic irrigation.

The patient should be given half a cat-unit of digitalis as early in the treatment as is practical. This safeguards her against edema of the

lungs. Finally she should be encouraged to drink plenty of water and lemonade. This is contrary to the teaching of certain well known neurologists* of Philadelphia, but I feel a great deal better when there is a good urinary output. If there is a tendency towards suppression of urine I usually give in addition 10 per cent glucose solution intravenously.

I have treated 121 eclamptics more or less in accordance with this simplified method: that is, by (1) prompt control of convulsions, (2) rest, (3) digitalis, and (4) water by mouth. I have had 6 maternal deaths. Two of these occurred early in the series before the importance of rest was recognized. They were given gastric lavage and colonic irrigations. Two were septic deaths. In one case, a cesarean section was done for contracted pelvis after the convulsions had been controlled. The patient died of peritonitis. The other patient died of pneumonia nine days postpartum.

The second point that this case brings up is the ultimate prognosis in cases of eclampsia and pre-eclampsia. There has been a recurrence of eclampsia in 7.5 per cent of my cases, and in even a larger percentage of cases there has been evidence of kidney impairment. Evans* has recently emphasized a group of unfavorable signs as follows: the existence of albuminuria for more than 14 days before delivery; a blood pressure over 170; persisting albuminuria after delivery; visual disturbances; and to a less extent, age of the patient and multiparity. The patients who have these signs, he says, are very apt to develop kidney trouble. The patient whom I have described had a high blood pressure and visual disturbances, but her urine cleared up promptly after delivery. Her age and parity were in her favor. Again I wish to emphasize the importance of bed rest. I do not believe that this patient could have carried the fetus to viability had she not stayed in bed 18 hours every day.

Dr. H. J. Stander, our guest in the Section on Obstetrics, has shown the importance of interrupting pregnancy at the first evidence of kidney involvement. I agree with him whole heartedly. In this case I did not wait for kidney function tests, but terminated the pregnancy as soon as the blood pressure went up and albumin was demonstrated in the urine.

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*Evans, Arwyn: The Late Effects of Toxemias of Pregnancy. Jour. Obst. & Gyn., Brit. Emp., 40:1024, 1933.

Southern Medical Journal

JOURNAL OF THE

SOUTHERN MEDICAL ASSOCIATION

Published monthly by the Southern Medical Association, Empire Building, Birmingham, Ala. Annual subscription $4.00. Single copies 35c each.

Entered as second-class matter at the Post Office at Birmingham, Ala., under Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1106, Act of October 3, 1917, authorized December 20, 1921.

M. Y. DABNEY, M.D., Editor
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Volume XXVII FEBRUARY 1934 Number 2

EDITORIAL DEPARTMENT

SOUTHERN MEDICAL ASSOCIATION
Twenty-Eighth Annual Meeting
San Antonio, Texas, November 13-16, 1934

TISSSUE CHANGES IN PREGNANCY

It was formerly believed that the physiological changes of normal gestation were confined chiefly to the breasts and genital tract. However, alterations in the cellular structure of the human ureters have been demonstrated, which result in a stiffening and rigidity of these organs, and which mechanically increase the tendency to stasis.[1] Gallstones are said to occur more frequently in pregnant women or in women who have borne children than in the nulliparous; and according to Levyn, Beck and Aaron,[2] in a series of late pregnancies in which gallbladder dye tests were done, failure of visualization was noted in a large proportion of cases.

Another characteristic and to some extent disabling change of gravidity occurs in the pelvic ligaments. According to the ancients, the pelvic joints softened during pregnancy,[3] so that the fetus could readily pass through. In modern animal husbandry, the "sinking of the rump" of the cow and her difficulty of locomotion show the veterinarian that she is near term.[3] The peculiar waddling gait seen in late human pregnancy is presumably due to the same cause, the relaxation of the ligaments which permits separation of the symphysis pubis. The same relaxation may be brought about in nonpregnant animals by corpus luteum extracts;[1] and a hormone has been standardized by its ability to effect this relaxation. A separation amounting to 0.9 centimeter in pregnant women, according to Bertin, of Philadelphia, may be taken as normal. Sometimes the pelvic relaxation is so great that it does not reverse itself after parturition. Orthopedic treatment in these cases usually gives marked improvement.

The changes in ureters, gallbladder and pelvic ligaments are probably compensated after delivery in most cases. They are mentioned to emphasize the need for protection during even a normal pregnancy, which is sometimes forgotten or belittled in this era of variegated activities of women.

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2. Levyn, L.; Beck, E. C.; and Aaron, A. H.: Further Cholecystographic Studies in the Late Months of Pregnancy. Amer. Jour. Roentg. & Ra. Ther., 30:774, Dec., 1933.

3. Bertin, E. J.: Separation of the Symphysis Pubis, with Report of Five Cases. Ibid, p. 797.

DIABETIC MORTALITY IN AMERICA AND ABROAD

With the discovery of insulin and its widespread use since 1922, it naturally has been expected that the death rate from diabetes would drop. Elliott P. Joslin, of Boston, Louis I. Dublin, statistician of the Metropolitan Life Insurance Company, and Herbert Marks,[2] of New York City, have compared the mortality from diabetes in this and other civilized countries in the past fifty years, and have brought out some unexpected facts.

Fifteen years ago, death from diabetes was infrequent. At the beginning of the century this disease ranked twenty-seventh among the causes of death. Now, although the mortality in childhood has decreased, the total rate in the population is notably greater. In the last three decades diabetes has advanced to tenth in importance as a cause of death among women in the United States. In Massachusetts in

1. Hisaw, F. L.; and Leonard, S. L.: Relation of the Follicle and Corpus Luteum Hormone in the Production of Progestational Proliferation of the Rabbit Uterus. Amer. Jour. Physiol., 92: 574, 1932.

2. Joslin, Elliott P.; Dublin, Louis I.; and Marks, Herbert H.: Characteristics and Trends of Diabetes Mortality Throughout the World. Amer. Jour. Med. Sci., 186:753, Dec., 1933.

1930, it was ninth. Twenty-six out of every 1,000 girl babies born in the United States are now expected to succumb to diabetes. The diabetic death rate in Canada is only two-thirds that of the United States. The rate in this country, say Joslin, Dublin and Marks, is the highest in the world.

Figures on comparative international death rates, such as these, which have been assembled by the most expert statisticians, cannot fail to arouse a number of questions. The obstetrical mortality of the United States[1] has also been widely publicized as one of the highest in the world. Possible deductions from these data are either that American medical service as far as diabetes and pregnancy are concerned is the worst in the world, or that Americans are more susceptible than any other people to these particular difficulties. The analysis under discussion shows that the incidence of diabetes is higher in Massachusetts and New York than in other states of the Union. It also notes that in these two states the "quality of medical certification" is the best in the country. The coincidence of high diabetic death rate and high quality of medical certification cannot fail to support the impression that the quality of medical certification considerably weights the diabetic death rate of any country; that a perceptible portion of the apparent rise in America and elsewhere may be the result of better training of physicians in the diagnosis of diabetes, and their increasing interest in the disease since the discovery of a specific therapy.

The increase in diabetic deaths is noted chiefly among older persons; the deaths of diabetic children have markedly decreased. The past third of a century has seen an increasing efficiency of public health work, which has protected the population from infectious diseases hitherto common. No doubt many persons of weak constitution who could not have survived an attack of typhoid fever, small pox, diphtheria, or diarrhea of infancy, have lived to swell the death rate of older persons from metabolic diseases. A great many factors must be taken into consideration before one attempts to explain mortality statistics. Diabetes is evidently very much to be looked for today among persons past middle life.

1. Editorial, Honesty in Puerperal Mortality Rates. Amer. Jour. Obst. & Gyn., 23:603, 1932.

GLEANINGS FROM RECENT JOURNALS

Gold in the Skin.—The two monetary metals, gold and silver, have long been known to have an antibacterial action. Intravenous injection of gold compounds for tuberculosis of the lungs and skin have been employed sporadically for a century and rather extensively since about 1913.[1] Colloidal gold, gold chloride, gold potassium cyanide, and synthetic salts were tried. In 1924, Mollgaard, of Denmark, published a book dealing with the treatment of tuberculosis by intravenous injections of gold sodium thiosulphate, "sanocrysin," and his preparation has since that time been rather popular, much more so in England and abroad than in the United States.[2] In 1927, its effect on lupus erythematosus was investigated by Schamberg and Wright,[1] of the University of Pennsylvania, and their favorable report was shortly thereafter rather widely confirmed.[3] A specific for this *bete noir* of dermatology was welcomed. Many injections of gold have since been administered for skin lesions of various types.

The fate of gold in the body has been in some question. It is claimed by certain investigators that it is excreted in the urine. Wigley,[4] of England, says that only rarely does it accumulate in the skin. Gaul and Staud,[5] of New York City, have published data to the contrary. They describe a spectroscopic technic for the measurement of minute amounts of the precious metal in small sections of the skin which may be removed at biopsy. The integument of untreated persons, they say, contains no gold discoverable by their method; but gold is always present in the cutis of persons who have received the therapeutic injections, and the amount detected is proportional to the total dosage, even if the patient is examined several years after treatment. The deposition of the precious metal in the skin, according to Gaul and Staud, is permanent.

1. Schamberg, J. F.; and Wright, Carroll S.: Use of Gold and Sodium Thiosulphate in the Treatment of Lupus Erythematosus. Arch. Dermat. & Syph., 15:119, 1927.

2. Editorial, Assessment of Sanocrysin. Lancet, 221:1362, 1931.

3. Whitehouse, H. H.; and Bechet, P. E.: Lupus Erythematosus, Lupus Vulgaris, Tuberculids and Tuberculosis of the Skin: Treatment with Gold Compounds. Arch. Dermat. & Syph., 16:563, 1927.

4. Wigley, J. E. M.: Deposition of Gold in the Skin. Brit. Jour. Dermat., 44:69, Feb., 1932. Abst. Arch. Dermat. & Syph., 27:331, 1933.

5. Gaul, L. E.; and Staud, A. H.: Clinical Spectroscopy: A Study of Biopsy Material Taken from Patients Receiving Gold Sodium Thiosulphate. Arch. Dermat. & Syph., 28:790, Dec., 1933.

If their results are confirmed, one will be left to wonder what effect this durable thin gold plating may have upon subsequent skin infections: for example, impetigo or the mycoses.

Prevention of Boils.—Schultz and Gebhardt[1] report an epidemic of boils among army saddle horses at Stanford University. It was not affected by ordinary autogenous vaccines, but was controlled by inoculation of the animals with a specific staphylococcus bacteriophage. They claim no curative effects from the bacteriophage treatment, only preventive. They agree with Larkum,[2] who has reported successful results in the arrest of human furunculosis by the same means: that probably the bacteriophage solution, which contains unheated bacterial protein, offers a vaccine of antigenic value superior to any of the killed cultures in clinical use.

Late Congenital Syphilis.—Prenatal clinics have emphasized the importance to the next generation of intensive treatment of the syphilitic woman.[3] Adequate early care of the mother will usually prevent lues in the fetus, the results being proportional to the period of gestation at which antisyphilitic therapy is begun;[4] and this preventive method gives so much better results than treatment of infants and children born with stigmata of the disease, that the results of therapy in congenital syphilis have received comparatively much less statistical attention. Smith,[5] of the Johns Hopkins Hospital Clinic, has analyzed the results in a series of congenital syphilitics treated after they were thirteen years of age, none of whom had received adequate care in the early stages of the disease.

In nearly half the patients the blood Wassermann remained positive under antisyphilitic therapy in spite of improvement of symptoms. Wassermann-fastness, or Wassermann reversal, had no relation to clinical improvement, and good therapeutic response was obtained in many patients whose Wassermann remained positive. More females than males attended the clinic, which was interpreted as meaning that in young males the mortality of congenital syphilis is higher than in females. Treatment even in this late stage tended to prevent the development of interstitial keratitis and nerve deafness. This is in confirmation of the earlier report of Robinson[1] from the same clinic, that after interstitial keratitis has been observed in one eye, adequate treatment may prevent its development in the other.

The evaluation of therapy from the Hopkins congenital syphilis clinic is slightly more encouraging than medical opinion generally has been as to this stage of lues.

Survival without Suprarenal Glands or Hormone.—The death of an animal from which the suprarenal glands are removed is considered a matter of a few days, unless one of the recently purified cortical extracts is supplied. Early attempts to maintain patients with Addison's disease by administering a large amount of sodium chloride were unsuccessful, though an occasionally good clinical result by this means is reported. A characteristic lowering of blood sodium has been noted after suprarenalectomy. Other salts, from recent studies, are also lost in large quantities. According to Rubin and Krick,[2] there is a negative balance, or severe drainage from the body, not only of sodium and chlorine, but also of calcium, magnesium, potassium, phosphorus and nitrogen. Considering that the loss of these elements might explain the symptoms of suprarenal insufficiency, the Philadelphia workers supplied them in considerable quantity in the drinking water and noted rapid improvement even of animals in a critical condition. Health was maintained for several months by this means.

The finding is somewhat contrary to generally observed physiological principles, since the loss of an element from the body means usually inability to utilize it. The diabetic who loses sugar in his urine is unable to metabolize carbohydrate and increase of the intake does not alleviate his symptoms.

Studies of the utilization or loss of the dietary components after gland extirpation offer the most promising lead to endocrine diagnosis and therapy.

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2. Larkum, N. W.: Ibid, 30:1395, 1933, quoted by 1.

3. McCord, J. R.: Syphilis and Pregnancy. Sou. Med. Jour., 23:40, 1930.

4. Reinberger, J. R.; and Toombs, P. W.: The End Results of Ten Years' Study of Treatment of Pregnancy Syphilis in Trimesters. Sou. Med. Jour., 26:532, 1933.

5. Smith, Frank R., Jr.: Late Congenital Syphilis: A Study of the Results of Treatment in 267 Patients. Bull. Johns Hopkins Hosp., 53:231, Nov., 1933.

1. Robinson, H. M.: Interstitial Keratitis in Late Congenital Syphilis. Sou. Med. Jour., 25:956, 1932.

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TWENTY-FIVE YEARS AGO
FROM JOURNALS OF 1909

Benzoate of Soda.[1]—"The referee board appointed by President Theodore Roosevelt to review some of the decisions made by the Bureau of Chemistry, according to press reports, has reversed the findings of Dr. Harvey W. Wiley regarding the harmfulness of benzoate of soda as a food preservative."

"Ultimatum to Insurance Companies.[2]—The physicians of Elbert County, Georgia, with one exception, have agreed that, beginning March 1, they will not make examinations of any kind for any insurance company for less than $5."

Control of Hemorrhage.[3]—"In . . . a patient operated upon for uterine fibroma in whom hemorrhage occurred owing to a ligature slipping, M. Chaput [of Paris] was easily able to gain command of the hemorrhage by the use of gelatin. . . . In cases of secondary hemorrhage, instead of following the usual course of opening up the wound at once, M. Chaput advises the use of a subcutaneous injection of gelatin. . . . Blood, of which the ordinary coagulation period is seven minutes, clots in three minutes after an injection of gelatin. . . . The method is very useful in cases of ruptured tubal pregnancy."

Useful Drugs.[4]—"If we attempt to sift out of the vast array of remedies only those which we today consider of importance, the number is not great. Most of the heavy metals are present, being represented by mercury, iron, arsenic, antimony and others and dating back to the dawn of medicine. From about the same period, and probably derived from Egyptian or Chinese medicine, we have opium and squills. Ipecac and cinchona are much more recent, dating from the Seventeenth Century, while digitalis, nux vomica and aconite appeared in the Eighteenth. Belladonna was known mainly as a poison, being little used in medicine. Alcohol, of course, must not be forgotten. . . .

"This short list of about a dozen drugs contains practically all of those which we today would consider in the first rank."

Sanitation in Manila Under United States Control.[5]—"At the time of the fall of Manila, August 13, 1898, it is safe to say that the sanitary situation in that city was as bad as any ever maintained by a civilized nation. . . .

"When we arrived in Manila the water supply was insufficient and of the poorest quality; and there were no sewers or other methods for the disposition of waste. The water supply for Manila was obtained from the Mariquina River a few miles from the city, the pumping station being kept supplied by a small dam sloping to an intake. Some idea of the condition of this water may be imagined from the fact that there were more than 20,000 people and half as many animals living on the banks of this river above the dam and that a great public highway passed along its banks for miles, many times crossing the stream, over which there was an enormous traffic of all kinds. The intake was guarded by a grate, and it was often necessary to remove the carcasses of dead and decomposing animals from in front of it in order that a fuller flow of water might reach the pumps. . . .

"I have many times seen persons with smallpox pustules not yet dry on their bodies attending to their stalls in the public markets, and have noticed tailors and cooks performing their duties while suffering from advanced and well-marked leprosy. . . .

"Finally, the population, on the whole, was ignorant, indifferent and even antagonistic toward any change in these conditions. . . .

"I am perfectly justified in saying that in ten years America has made Manila one of the cleanest, healthiest and most attractive cities under the flag, and that if the present rate of improvement continues other American cities will have to look to their laurels."

1. Editorial, Dr. Wiley and Benzoate of Soda. J.A.M.A., 52:562, 1909.
2. State News, J.A.M.A., 52:566, 1909.
3. Gulf States Journal of Medicine and Surgery, 14:112, 1909, quoting Lancet, Dec. 12, 1908.
4. Edmunds, C. W.: Therapeutic Progress. J.A.M.A., 52: 519, 1909.
5. Musgrave, W. E.: Ten Years of American Sanitation in the Philippine Islands. J.A.M.A., 52:442, 1909.

Correspondence

WANTED: DATA ON WOMEN IN MEDICINE

Editor, SOUTHERN MEDICAL JOURNAL:

I am collecting in book form data about women, and the work of women, in the field of medicine. I have already secured a number of portraits, books and pamphlets from the United States and Great Britain, and will be grateful for information concerning additional material suitable for my collection, which I plan to give, when completed, to the Library of the Tulane University School of Medicine. A special book-plate is being planned.

I am particularly desirous of securing information, both in manuscript and print, having to do with medical women in the South. The idea of special collections on different subjects will perhaps be of interest to others.

ELIZABETH BASS, M.D.

1430 Tulane Avenue,
New Orleans, Louisiana, December 19, 1933.

Book Reviews

Treatment of the Commoner Diseases Met with by the General Practitioner. By Lewellys F. Barker, M.D., Professor Emeritus of Medicine, Johns Hopkins University: Visiting Physician, Johns Hopkins Hospital, Baltimore, Maryland. 319 pages. Philadelphia, Pennsylvania: J. B. Lippincott Company, 1934. Cloth, $3.00.

No man since Osler has stirred the imagination of physicians or stimulated them in the study and practice of scientific medicine more than Lewellys F. Barker, Osler's successor as Professor of Medicine in Johns Hopkins Medical School. Dr. Barker has written many books. Indeed, he has been perhaps the most prolific writer in the field of medicine in the Twentieth Century. It is probable that his latest publication, in the year 1934, entitled "Treatment of the Commoner Diseases Met with by the General Practitioner," will be the most widely read and the most useful book that has come from his facile dictaphone. It is said that Dr. Barker's knowledge is so coordinated, classified and card indexed in his brain cells that the copy from his dictaphone rarely has to be corrected.

The opening chapter on *Advances in the Methods of Studying Patients* presents a dissertation on the philology of bodily characteristics, from which the reader will become familiar with such choice words as pyknic, leptosome and diplastic as descriptive of types of individuals the physician meets with in daily practice. In the same chapter the psychologic technic in studying the patient, in which Dr. Barker is pastmaster, is beautifully delineated.

The chapter on commoner disorders of the circulatory system presents a brief summary of the treatment of diseases of the heart and blood vessels. The newer therapy of the anemias, the diseases of the gastro-intestinal tract, the liver, gallbladder and urinary passages is covered in several chapters. If any two chapters are stronger than the others they are those discussing the management of the commoner nervous and mental diseases and disorders of the endocrine system. Included in the latter are "hypoinsulinism (diabetes mellitus)" and "hyperinsulinism," which Dr. Barker considers as disorders of insulin secretion.

Probably no man in medicine is more familiar with medical literature than Dr. Barker; and a valuable feature of this distinctive Barkerian monograph is the bibliography.

It is an illuminating epitome of knowledge gained from forty years of study of patients and the science of medicine.

A Text-Book of Physiology. By William H. Howell, Ph.D., M.D., Sc.D., LL.D., Emeritus Professor of Physiology in the Johns Hopkins University, Baltimore, Maryland. Twelfth Edition, thoroughly revised. 1132 pages with 308 illustrations. Philadelphia and London: W. B. Saunders Company, 1933. Cloth, $7.00 net.

Since the first edition in 1905 this has been a standard text-book. None of the medical sciences has gone faster than physiology in its development through research in the past twenty-eight years. Considerable rewriting and revision have kept it up to date. The author acknowledges a great deal of help from specialists in the many special lines of investigation.

The subject matter is divided into: physiology of muscle and nerve; of the central nervous system; the special senses; respiration; digestion and secretion; nutrition and heat production and regulation; with a rather brief concluding section on reproduction.

The 1933 Year Book of Radiology. Diagnosis, Edited by Charles A. Waters, M.D., Associate in Roentgenology, Johns Hopkins University; Assistant Visiting Roentgenologist, Johns Hopkins Hospital. Therapeutics, Edited by Ira I. Kaplan, B.Sc., M.D., Director, Division of Cancer, Department of Hospitals, City of New York. Clinical Professor of Surgery, New York University and Bellevue Medical College. 804 pages, with 780 illustrations. Chicago: The Year Book Publishers. Cloth, $7.00.

The second edition of this publication is similar in its presentation to the 1932 volume. About equal parts are devoted to diagnosis and therapy, each subject being grouped under the body system involved. It is more comprehensive than its predecessor; is 54 pages larger; contains 282 more contributions (690 in all) chosen from 125 scientific publications in 19 countries. The book is not by any means a haphazard collection, but contains abstracts carefully selected and correlated.

The following additional sections have been added to the division on diagnosis: hematopoietic system, skull, sinuses and mastoids; obstetrics and gynecology; and historical. The authors have excelled the former volume. The book represents work as well as knowledge. It is hoped that the authors will make it an annual publication.

Office Surgery. By Fenwick Beekman, M.D., Visiting Surgeon, Bellevue Hospital; Clinical Professor of Surgery, New York University and Bellevue Medical College. 402 pages, illustrated. A volume of the Everyday Practice Series, Edited by Harlow Brooks, M.D. Philadelphia and London: J. B. Lippincott Company, 1932. Cloth, $5.00.

Dr. Beekman discusses the materials needed for surgery in the office, such as slings, bandages, drains and dressings. For anesthesia, local receives first place, as it can be given without assistance and its duration is sufficient for most office procedures. A wound is defined as a solution in the continuity of the tissue, the result of violence. Wounds are classified according to location and type. No mention is made of the prophylactic use of gas gangrene serum, although antitetanus serum is advised in wounds contaminated with dust and dirt. Fractures and dislocations are frequent conditions observed in office practice and careful consideration is given to methods of reduction, splinting and after-care.

Among the simple infections described are abscesses, carbuncles and furuncles. Those which are found in special areas, as peritonsillar abscesses, Ludwig's angina, felons, palmar infections and ingrown toe nails are described separately.

The writer feels that all surgery should be done in a fully equipped hospital. The subject matter is confined to diseased conditions which are on the surface of the body or accessible through the natural openings. A great many practical hints as to diagnosis and treatment make this text valuable to the practitioner.

A Text-Book of Medicine. (By 141 American Authors.) Edited by Russell L. Cecil, A.B., M.D., Sc.D., Professor of Clinical Medicine, Cornell University Medical College; and Associate Editor for Diseases of the Nervous System, Foster Kennedy, M.D., F.R.S.E., Professor of Neurology, Cornell University Medical College. Third Edition, Revised and Entirely Reset. 1664 pages, illustrated. Philadelphia and London: W. B. Saunders Company, 1933. Cloth, $9.00 net.

In this book one will find references to practically every human ailment. Since the publication of the last edition several of the contributors have died. The sections with which they were identified have been entirely rewritten. Among the new articles are those on plague, kala-azar, psittacosis, rat-bite fever, pertussis, the erythemas, poisoning by radio-active substances, diseases of the bronchi, hypotension, diabetes mellitus, diseases of the parathyroids, disease of the suprarenal system, diseases of the pituitary body. At the end of each article an extensive bibliography is given. It is one of the best texts on medicine.

Final Report of the Commission on Medical Education. 560 pages. New York: Office of the Director of Study, 1932.

An inquiry into medical education was started in 1925 with the inception of this Commission. This is the final report of that body. In the intervening seven years various *ad interim* reports and supplementary studies have been published, which are included in this volume. Among the conclusions reached are: a satisfactory medical program is essential to modern community life; there is need for better correlation of cases referred to specialists; the economic and social problems give rise to the factor of national sickness insurance and there is an oversupply of physicians in the country, which is being added to each year. A large appendix contains many tables of interesting data.

Southern Medical News

HONORS FOR DR. MOORE, THE PRESIDENT

Dr. Hugh Leslie Moore, Dallas, Texas, elected President of the Southern Medical Association at its last annual meeting in November, was tendered a testimonial dinner at the Dallas Country Club on Friday evening, January 5, the dinner being sponsored by the Dallas County Medical Society and the Woman's Auxiliary of the Dallas County Medical Society. Dr. Elbert Dunlap, Dallas, member of the Council of the Southern Medical Association from Texas, was toastmaster, being introduced by Dr. F. H. Newton.

Hon. Pat Neff, a former governor of Texas, and now President of Baylor University, Waco and Dallas, made the principal address of the evening, being introduced by Dr. Edward H. Cary, a past president of the Southern Medical Association and of the American Medical Association. Addresses were also made by Dr. Holman Taylor, Fort Worth, Secretary of the Texas State Medical Association; by Colonel C. C. Walsh, of the Federal Reserve Bank of Dallas, on "The Physician as a Citizen"; and by Mrs. Charles L. Martin, Dallas, President of the Woman's Auxiliary, on "The President's Wife."

Dr. C. M. Rosser, for those assembled, presented Dr. Moore with a bronze plaque. Dr. Moore responded pleasingly and feelingly. The plaque reads as follows: "Presented to Hugh Leslie Moore, M.D., by his friends, commemorating his elevation to the Presidency of the Southern Medical Association. January 5, 1934." Dr. Hall Shannon was in charge of the entertainment program for the evening.

Some two hundred physicians and friends and their ladies honored Dr. Moore by their presence at this testimonial dinner.

At the regular meeting of the Dallas County Medical Society, Dallas, Texas, on Thursday evening, December 14, 1933, the following resolution was adopted:

"WHEREAS, The Southern Medical Association at its recent meeting at Richmond, Virginia, in the exercise of a discriminating judgment, selected one of our distinguished and much loved members, Dr. Hugh Leslie Moore, as its forthcoming president;

"THEREFORE, BE IT RESOLVED, That the Dallas County Medical Society, in grateful acknowledgment of its appreciation, felicitates itself upon the honor thus conferred, congratulates Dr. Hugh Leslie Moore upon his merited preferment, and extends to the Southern Medical Association this evidence of its appreciation."

THE SOUTHEASTERN SURGICAL CONGRESS

The Southeastern Surgical Congress will hold its fifth annual assembly at Nashville, Tennessee, Monday, Tuesday and Wednesday, March 5-7, 1934. The Andrew Jackson Hotel will be hotel headquarters, and the scientific presentations and exhibits will be in the War Memorial Building just in front of the hotel. Dr. Willis Campbell, Memphis, is President, and Dr. B. T. Beasley, 1019 Doctors Building, Atlanta, Georgia, is Secretary. A helpful and interesting scientific program has been arranged, presentations to be made by physicians of national and international reputation.

MID-SOUTH POST-GRADUATE MEDICAL ASSEMBLY

The Mid-South Post-Graduate Medical Assembly, until 1931 the Tri-State Medical Association of Mississippi, Arkansas and Tennessee, will hold its semi-centennial meeting in Memphis, Tennessee, on Tuesday, Wednesday, Thursday and Friday, February 13-16, 1934, at the Hotel Peabody. Dr. F. J. Runyon, Clarksville, Vice-President for Tennessee, will preside, having acted as President since the death last June of the President, Dr. A. B. Dancy, of Jackson, Tennessee. Dr. P. W. Rowland, of Oxford, Mississippi, a charter member of the Association, is the President-Elect. Dr. Augustus Street, Vicksburg, is Vice-President for Mississippi, and Dr. H. King Wade, Hot Springs, is Vice-President for Arkansas. Dr. A. F. Cooper, 10 South Main Street, Memphis, is Secretary-Treasurer. The program committee is composed of Dr. Richard C. Bunting, Chairman, Dr. J. L. McGehee, Dr. J. A. Crisler, Jr., and Dr. Conley H. Sanford, all of Memphis. Dr. Gilbert Levy, Memphis, is director of exhibits. A feature of the meeting will be the stag buffet supper at the Memphis Country Club, tendered by the medical profession of Memphis on Wednesday evening. A helpful and interesting scientific program has been arranged, presentations to be made by physicians of national and international reputation.

ALABAMA

The Marengo County Medical Society met recently for dinner and a special session. Talks were made by Mrs. Ethel H. Crumpton, County Social Service Director, Mrs. Janie Harrison, County Health Nurse, and Dr. E. B. Bailey, Demopolis. Dr. E. T. Norman, Linden, County Health Officer, arranged for the dinner.

The Bryce Hospital was host to the Tuscaloosa County Medical Society recently at a turkey dinner, followed by a scientific program.

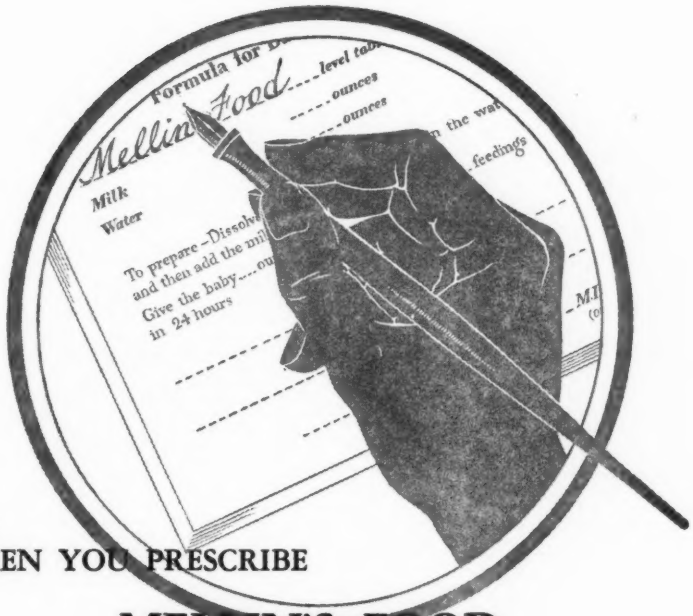
Dr. H. Earle Conwell, Fairfield, was on the program of the Clinical Congress of the Connecticut State Medical Society held at Yale University Medical School, New Haven, Connecticut.

The Baldwin County Medical Society has unanimously elected the following officers for the coming year: Dr. W. C. Holmes, Foley, President; Dr. J. C. McLeod, Bay Minette, Vice-President; and Dr. J. Chason, Bay Minette, Secretary-Treasurer.

ARKANSAS

Physicians of Ashley, Chicot, Desha and Drew Counties met at McGehee in November and organized the Southeast Arkansas District Medical Society, the following officers being elected for the coming year: Dr. H. T. Smith, McGehee, President; Dr. J. S. Wilson, Monticello, Vice-President; and Dr. M. C. Crandall, Wilmot, Secretary.

Continued on page 22



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Literature and Samples of Mellin's Food Gladly Supplied — to Physicians

Continued from page 184

The Sixth Councilor District Medical Society, organized at a meeting at DeQueen in November, has elected the following officers for the coming year: Dr. R. R. Kirkpatrick, Texarkana, President; Dr. C. E. Kitchens, DeQueen, Vice-President; and Dr. C. A. Archer, DeQueen, Secretary-Treasurer.

Dr. Walter Eberle and Dr. Everett Moulton, both of Fort Smith, did some postgraduate work in comparative anatomy during November.

Dr. W. J. Curry, Rogers, who has been a member of the Rogers Masonic Lodge for 44 years, was a guest of honor at a meeting of the Lodge recently.

Dr. C. S. Holt, Fort Smith, was recently reappointed a Trustee of the Arkansas Tuberculosis Sanitarium.

Dr. Guy Hodges, Rogers, has been elected a director of the Chamber of Commerce.

Dr. William H. McCarroll, Walnut Ridge, has received his degree from the University of Tennessee Medical College, and is now making a trip to South American countries as ship surgeon.

DEATHS

Dr. Grover Cleveland Webb, Russellville, aged 40, died November 27.

Dr. Charles E. Wright, Gurdon, aged 62, died November 30 of cerebral hemorrhage.

Dr. Daniel J. Halbrook, Formosa, aged 61, died November 28 of heart disease.

Dr. J. M. McLendon, Gould, aged 74, died November 20 of carcinoma.

DISTRICT OF COLUMBIA

The Fairfax County (Virginia) Medical Society met in Washington at the Racquet Club recently for its quarterly meeting, with Dr. George B. Trible, Washington, acting as host.

The District of Columbia Medical Society's Section on Ophthalmology and Otolaryngology met in December at the Johns Hopkins Hospital, Baltimore, for a joint session with the Section on Ophthalmology and Otolaryngology of the Baltimore City Medical Society.

At the regular meeting in December of the Medical Society of the District of Columbia the program was furnished by the Baltimore-Washington Urological Society.

The George M. Kober Medical Society, Washington, has elected the following new officers for the coming year: Dr. Tomas Cajigas, President; Dr. Ernest E. Hadley, Vice-President; Dr. Herbert H. Schoenfeld, Secretary; and Dr. Howard L. Smith, Treasurer; all of Washington.

A series of clinics and demonstrations is announced for February 23 and 24, to be given at Gallinger Municipal Hospital and other institutions, this to be coincident with the annual homecoming of graduates of the George Washington University School of Medicine.

DEATHS

Dr. Noble Price Barnes, Washington, aged 62, died November 26 of cerebral hemorrhage.

Dr. Emmett Emerson Newcomer, Washington, aged 41, died November 25.

FLORIDA

Dr. Clyde O. Anderson has located at St. Petersburg, having opened offices with his father in the Hassler Building, after completing his internship in the Tampa Municipal Hospital.

The Dade County Medical Society has elected the following officers for the coming year: Dr. Roy J. Holmes, President; Dr. F. A. Vogt, Vice-President; Dr. Robert T. Spicer, Secretary; and Dr. H. A. Barge, Treasurer; all of Miami.

The Duval County Medical Society at a recent meeting elected the following officers for the coming year: Dr. Theodore G. Croft, President; Dr. William S. Manning, Vice-President; Dr. B. F. Woolsey, Secretary; and Dr. J. W. Hayes, Treasurer; all of Jacksonville.

The Florida East Coast Medical Association met at Coral Gables recently and elected the following officers for the coming year: Dr. Leigh F. Robinson, Fort Lauderdale, President; and Dr. Spencer A. Folsom, Orlando, Secretary-Treasurer.

The Leon-Gadsden-Liberty-Wakulla-Jefferson County Medical Society has elected the following officers for the coming year: Dr. J. H. Pound, Chattahoochee, President; Dr. J. K. Johnston, Tallahassee, Vice-President; and Dr. O. G. Kendrick, Tallahassee, Secretary-Treasurer.

The Tallahassee Medical Club has elected the following offi-

Continued on page 24

HARVARD MEDICAL SCHOOL

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General Course in Orthopaedic Surgery

PROFESSOR OBER and associates: Wards and Out-Patient Departments of Children's Hospital; ASSISTANT PROFESSOR SMITH-PETERSEN and associates: Massachusetts General Hospital; and the Anatomical Laboratory, Harvard Medical School.

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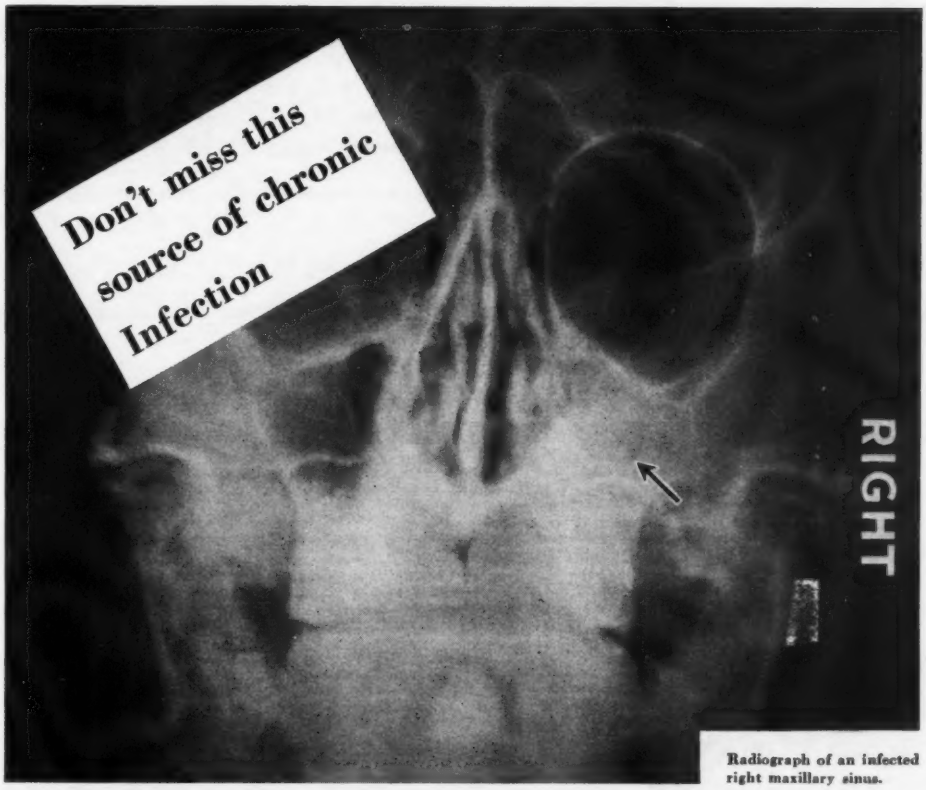
Given for eight or more students. Women admitted only to clinical and didactic work.

Fee, $200.

For further information apply to Assistant Dean, Courses for Graduates, Harvard Medical School, Boston, Massachusetts.



Radiograph of an infected right maxillary sinus.

CHRONIC sinusitis often causes perplexing symptoms of disorders in unrelated organs. Among the most common are stubborn disturbances of the respiratory and gastro-intestinal systems. Particularly in children, such conditions can be produced by the aspiration or swallowing of pus from infected sinuses.

When you encounter such situations, the most effective way to confirm or rule out the sinuses as a focus of infection is by x-ray examination. If your clinical findings do not provide satisfactory information upon which to base an opinion, refer the patient to your radiologist for a radiographic survey.

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Offices in Most Principal Cities

Continued from page 22

cers for the coming year: Dr. J. K. Johnston, President; Dr. M. F. Boyd, Vice-President; and Dr. O. G. Kendrick, Secretary and Treasurer; all of Tallahassee.

Dr. J. A. Stanford, Fort Lauderdale, who has been away for the past two years, has returned and opened offices in the Sweet Building.

Dr. Lawrence Simcox, St. Petersburg, has moved into new offices at 201 Third Street, North.

Dr. C. L. Davis, Okeechobee, took postgraduate work in surgery at Tulane University, New Orleans, recently.

Dr. Jack Halton, formerly of Sarasota, has located at Tampa with offices in the Citizens' Bank Building.

Dr. Robert Elmer Summitt, Gainesville, and Miss Willie May Lang were married recently.

Deaths

Dr. Cole Carroll, Apopka, aged 48, died November 9 of acute dilatation of the heart.

Dr. William Jackson Cole, South Miami, aged 83, died November 10.

Dr. Albon Ellsworth Bartoo, Pomona, aged 71, died November 30 of heart disease.

GEORGIA

The Emory University Hospital Staff has elected the following new officers for the coming year: Dr. Lewis M. Gaines, President; Dr. Lon Grove, Vice-President; and Dr. J. D. Martin, Secretary; all of Atlanta.

Dr. W. H. Powell, Lumber City, and Dr. J. M. Oliver, Hazlehurst, have established the Cor De Lois Hospital at Hazlehurst, which consists of laboratory, x-ray, operating room, etc., for the diagnosis and treatment of diseases.

Dr. R. C. Swint, Milledgeville, has been reelected Superintendent of the Milledgeville State Hospital.

Dr. E. J. Smith and Dr. J. R. Smith, Hahira, were hosts recently to the members of the Lowndes County Medical Society.

Dr. D. M. Bradley and Dr. W. F. Reavis, Waycross, were hosts at dinner recently to members of the Ware County Medical Society and their wives.

Dr. W. H. Scruggs has returned to his former home, Waycross, and opened offices for the private practice of medicine, having been formerly stationed at Marine Hospital No. 11, Louisville, Kentucky.

Dr. William C. Williams, Jr., Macon, has opened offices in the Bibb Building with practice limited to urology.

Dr. Eugene E. Murphey, Augusta, has been elected to succeed Dr. H. W. Shaw, deceased, as a member of the Board of Trustees of the University Hospital.

Dr. B. W. Greene, Macon, is the newly elected City Physician; and Dr. James T. Ross, Macon, has been chosen Assistant City Physician.

Dr. D. S. Reese, Carrollton, was recently elected to the Board of Trustees of the Georgia Baptist Hospital, Atlanta.

Dr. and Mrs. J. H. McClure, Cornelia, were hosts recently to members of the Habersham County Medical Society and their wives.

The Management of the Franklin Hospital, Swainsboro, announces the association as Night Supervisor of Miss Mary Cornett, formerly with the Macon Hospital.

Dr. S. B. Strong, Major, M.C., U. S. Army, was recently called to active duty and stationed at Fort Oglethorpe, with the assignment of general surgery in the Station Hospital.

Dr. Louis O. Wootten, Cordele, and Miss Kathryn Royal were married recently.

Dr. Leo Smith, Pearson, and Miss Dorothy Elizabeth Quillian were married recently.

Dr. James Allen Smith, Macon, and Miss Sarah Jennings were married recently.

Dr. William Ray McGinty, Moultrie, and Mrs. Mynelle Marsh were married recently.

Dr. William E. Brown and Miss Sara Price, both of Macon, were married recently.

Deaths

Dr. Carlos Brown Meadows, Valdosta, aged 61, died December 8 of heart disease.

Dr. Thomas Byron Kea, Adrian, aged 54, died December 5 of heart disease.

Dr. Joseph Allen Wright, Covington, aged 80, died August 20 in an Atlanta hospital.

Dr. Nathaniel Pierce Walker, Milledgeville, aged 53, died November 20 of pulmonary tuberculosis.

Dr. Henry William Shaw, Augusta, aged 51, died October 27 of arterial hypertension and cerebral hemorrhage.

Continued on page 28

THROAT affections are usually more prevalent during winter months and the physician frequently needs alleviating agents.

Thantis Lozenges were developed for use in the treatment of infections and irritations of the throat and mouth.

The lozenges contain Merodicein, 1/8 grain, and Saligenin, 1 grain, and combine antiseptic and anesthetic action. Low toxicity of the two ingredients permits frequent use and therefore almost continuous treatment of the affected regions.

Physicians have found Thantis Lozenges effective in the treatment of acute throat infections. The lozenges are especially useful in relieving the pain following tonsillectomy and in reducing the infection by controlling the number and viability of pathogenic bacteria.

Literature and a sample package will be sent to physicians on request.

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White's Cod Liver Oil Concentrate Tablets are one of the oldest* stable, proven, potent, emulsifying *concentrates of cod liver oil on the market. Their efficacy and scientific soundness are attested by clinical tests in recognized institutions. They stand accepted by the Council on Pharmacy and Chemistry of the American Medical Association.

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And eight years of intensive scientific research have produced what we consider the perfect cod liver oil concentrate. The potency of the actual concentrate used in the making of White's Cod Liver Oil Concentrate Tablets is approximately 150 times that of liquid cod liver oil—1000 vitamin A units (U.S.P.) and not less than 500 units of vitamin D (A.D.M.A.) per gram.

We put this highly potent concentrate in tablet form because the tablet is more palatable, infinitely more convenient. Its accuracy in dosage is beyond guesswork . . . no liquid to spill . . . no deterioration of vitamin potency.

Naturally, the real test of any medical product is how it works clinically. White's Cod Liver Oil Concentrate Tablets have been tested clinically in leading institutions. These tests have convincingly proved the merit of White's Cod Liver Oil Concentrate Tablets.

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On request, we shall send you a professional sample of White's Cod Liver Oil Concentrate Tablets. Also an interesting food chart which gives you the value of foods—vitamins, proteins, fats, carbohydrates, minerals—acid and alkaline reactions—all at a glance—just by revolving a wheel. Very convenient. Address Health Products Corporation, 113 N. 13th Street, Newark, N. J. Department B-4 Please use your prescription form or letterhead.

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The unique feature of Diodrast (formerly Neoskiodan) is that only a small amount of the drug, less than that of any other radiopaque substance, is required to obtain a wholly reliable skiagram. This is due to the fact that the kidneys rapidly excrete Diodrast in high concentration.

The intravenous injection of Diodrast is virtually painless and unattended by systemic reactions. Therefore it can be employed not only in adults but in children. It has been found to be well tolerated even in cases of serious systemic disease as well as during pregnancy. Practically the only contraindication is uremia or latent uremia.

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STERILE SOLUTION
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Supplied in convenient 20 and 10 cc. ampules ready for use.

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302M

Continued from page 24

Dr. Thomas M. McIntosh, Thomasville, aged 80, died December 4 of heart disease.

Dr. George R. Well, Monroe, aged 65, died November 26.

KENTUCKY

Dr. Will Maddux McClarin and Miss Emma Nan Harris, both of Louisville, were married December 16.

Dr. Levi Steely Siler, Corbin, and Miss Dorsie Pemberton were married recently.

Deaths

Dr. Robert Wallace, Louisville, aged 80, died December 1 of parenchymanephritis.

Dr. James McConnell Hubbard, Hickman, aged 70, died November 29 of heart disease.

Dr. John Shelby Moremen, Louisville, aged 68, died November 30 of angina pectoris.

Dr. Benjamin Franklin Zimmerman, Louisville, aged 60, died November 10 of heart disease.

Dr. Emilius Morancy McKee, Lexington, aged 57, died November 17 of carcinoma of the stomach.

Dr. Joseph Pryse Sutton, Kitts, aged 46, died suddenly November 6 of coronary thrombosis.

Dr. D. E. Burrow, Russellville, aged 58, died November 14 of cerebral hemorrhage.

LOUISIANA

Dr. Rudolph Matas, New Orleans, was recently presented by Luis Careaga, Spanish Consul, with the order of Isabel la Catolica, this being the sole Spanish decoration retained by the Spanish Republic from the late monarchy. The presentation was made before a gathering of the New Orleans consular corps, representatives of the Chamber of Commerce, and of the Orleans Parish Medical Society, and others.

The Baptist Hospital Staff and the New Orleans Obstetrical and Gynecological Society recently held a joint meeting.

The first award of the Rudolph Matas Medal for Vascular Surgery was presented recently to Dr. Mont R. Reid, Cincinnati, Ohio. The fund which provides for this award to be made to the "North American surgeon who has contributed outstanding work in vascular surgery" was created at the request of and in memory of a patient of Dr. Matas, and will be administered by Tulane University.

Dr. H. W. E. Walther, New Orleans, head of the Department of Urology at Southern Baptist Hospital, was a guest speaker in January at the joint meeting of the New York Division of the American Urological Association and the Section of Genito-Urinary Surgery of the New York Academy of Medicine.

The Staff of the French Hospital, New Orleans, recently elected the following officers for the coming year: Dr. J. J. Baron, Chairman; Dr. M. L. Stadiem, Vice-Chairman; and Dr. N. J. Tessitore, Secretary; all of New Orleans.

The Ascension Parish Medical Society has elected the following officers for the coming year: Dr. D. C. Brumfield, Darrow, President; Dr. T. H. Hanson, Donaldsonville, Vice-President; and Dr. Myer Epstein, Gonzales, Secretary-Treasurer.

The Claiborne Parish Medical Society has elected the following officers for the coming year: Dr. E. A. Campbell, Homer, President; Dr. L. T. Waller, Haynesville, Vice-President; and Dr. H. R. Marlatt, Homer, Secretary-Treasurer.

The DeSoto Parish Medical Society has elected the following officers for the coming year: Dr. R. A. Tharp, Mansfield, President; Dr. V. L. Sandifer, Logansport, Vice-President; and Dr. W. G. Jones, Mansfield, Secretary-Treasurer.

The East and West Feliciana Bi-Parish Medical Society has elected the following officers for the coming year: Dr. C. C. Blakeney, St. Francisville, President; Dr. J. B. Stanley, Jackson, Vice-President; and Dr. E. M. Toler, Clinton, Secretary-Treasurer.

The Iberia Parish Medical Society has elected the following officers for the coming year: Dr. Guy A. Shaw, President; and Dr. Henry Allen King, Secretary-Treasurer; both of New Iberia.

The Orleans Parish Medical Society has elected the following officers for the coming year: Dr. Waldemar R. Metz, President; Dr. Val H. Fuchs, First Vice-President; Dr. Edmund L. Leckert, Second Vice-President; Dr. Philip J. Carter, Third Vice-President; Dr. Frederick L. Fenno, Secretary; Dr. Walter P. Gardiner, Treasurer; and Dr. Alton Ochsner, Librarian; all of New Orleans.

The Pointe Coupee Parish Medical Society has elected the following officers for the coming year: Dr. J. F. Cazayoux, New Roads, President; Dr. J. W. Plauche, Morganza, Vice-President; and Dr. J. M. Mosely, Lakeland, Secretary-Treasurer.

The Rapides Parish Medical Society has elected the following officers for the coming year: Dr. H. Aubrey White, Alexandria, President; Dr. J. W. Phillips, Boyce, First Vice-President; Dr. R. P. Evans, Alexandria, Second Vice-President; Dr. D. B. Barber, Alexandria, Secretary-Treasurer.

The Red River Parish Medical Society has elected the following officers for the coming year: Dr. W. T. Wilkinson, Coushatta, President; Dr. L. S. Huckaby, Harmon, Vice-President; and Dr. W. W. Gahagan, Coushatta, Secretary-Treasurer.

The Terrebonne Parish Medical Society has elected the following officers for the coming year: Dr. R. W. Collins, President; Dr. J. B. Duval, Vice-President; and Dr. S. F. Landry, Secretary-Treasurer; all of Houma.

The Fourth District Medical Society has elected the following officers for the coming year: Dr. J. G. Yearwood, Gayle, President; Dr. Wilkins McDade, Minden, Vice-President; and Dr. Paul D. Abramson, Minden, Secretary-Treasurer.

The Fifth District Medical Society has elected the following officers for the coming year: Dr. C. C. Thompson, Delhi, President; Dr. J. S. McBride, Ansley, Vice-President; and Dr. John G. Snelling, Monroe, reelected Secretary-Treasurer.

MARYLAND

The Baltimore-Washington Urological Society furnished the program for a recent meeting of the Medical Society of the District of Columbia.

The Section on Ophthalmology and Otolaryngology of the Baltimore City Medical Society held a joint meeting at Johns Hopkins Hospital in December with the Section on Ophthalmology and Otolaryngology of the Medical Society of the District of Columbia.

Dr. Isaac Ridgeway Trimble and Miss Margaret Price Brown, both of Baltimore, were married recently.

Dr. Warde Baunton Allan, Baltimore, and Miss Angelica Peale Iglehart were married in December.

Dr. Frederick S. Wolf, Baltimore, and Miss Betty Saunders Stern were married recently.

Deaths

Dr. Donna Ann Waldran, Baltimore, aged 74, died December 11 of chronic nephritis and uremia.

Continued on page 30

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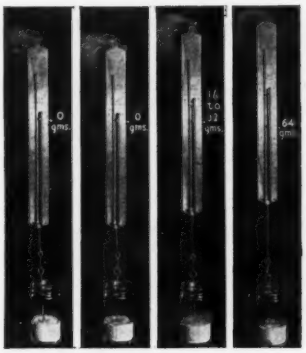

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Schematic drawing of the relative size of the curds of cow's milk and Similac vomited by six weeks old puppies after one-half hour's ingestion.

THE curds of milk contain only a small amount of carbohydrates, sufficient, however, to be a disturbing factor in infant feeding.

"A large part of the digestion and absorption of the carbohydrates takes place in the upper part of the small intestines." [1]

"The disaccharides, maltose, sucrose and lactose, are converted into monosaccharides through the action of enzymes secreted by the small intestine and are absorbed in the form of monosaccharides.

"When absorption is impaired, some sugar may reach the large intestine and here be attacked by the bacteria present. Sugar itself rarely appears in the stool, it being decomposed to form acids and gases." [2]

The large, tough curds of cow's milk are more slowly disintegrated and thus more slowly release the encased carbohydrates than the soft, flocculent curds of SIMILAC.

The disintegration of the curd of cow's milk may not be completed until after the curd, with the encased carbohydrate, has passed that portion of the small intestine where the enzymes for the conversion of disaccharides into monosaccharides are present. There is not this possibility when SIMILAC is fed because the fineness of the curd of SIMILAC does not permit of the encasement of carbohydrates to any extent.

The finer the curd the greater the surface area. The greater the surface area the more exposed are the fats, carbohydrates, proteins and salts to the digestive enzymes. Result . . . a more complete utilization of the food elements.

[1] London & Polowzowa: Zeitschr. f. physiol. Chem. 1906, XLIX, 328.

[2] Marriott: Infant Nutrition, pg. 81.

Samples and literature will be sent on receipt of your prescription blank.

SIMILAC—Made from fresh skim milk (casein modified); with added lactose, salts, milk fat and vegetable and cod liver oils.

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COLUMBUS, OHIO.

Continued from page 28

Dr. David Thomas Bowden, Jr., Leonardtown, aged 41, died suddenly November 2 of heart disease.

Dr. Mactier Warfield, Baltimore, aged 75, died November 2 of carcinoma.

Dr. Howard C. Silver, Baltimore, aged 73, died October 22.

Dr. Stanley White Barber, Gaithersburg, aged 55, died November 19.

MISSISSIPPI

The following Mississippi physicians have been awarded fellowships for graduate study by the Commonwealth Fund, and have entered Tulane University, New Orleans: Dr. C. E. Boyd, Amory; Dr. George Barnes, Belzoni; Dr. T. F. Clay, Tutwiler; Dr. E. F. Hand, Waynesboro; Dr. A. B. Harvey, Tylertown; Dr. F. L. McGahey, Calhoun City; Dr. S. B. McIlwain, Pascagoula; Dr. M. L. McKinnon, Lauderdale; Dr. W. B. Shackleford, Hollandale; Dr. J. C. Wallace, Osyka; Dr. D. L. Walker, Meridian; Dr. J. T. Weeks, Biloxi; Dr. Dudley Stennis, Newton; Dr. A. P. Smith, Bay St. Louis; Dr. H. E. Frizell, Vaughn; and Dr. H. G. Johnson, Dundee.

Dr. Gladys Ratcliff, McComb, has been appointed Editor for Pike County.

Dr. Robert B. McLean, formerly of Greenwood, but more recently of New York, has opened offices in the Lamar Life Building, Jackson, for the practice of surgery.

Dr. L. C. Davis, Greenville, is the newly elected President of the Kiwanis Club of his city.

Dr. H. B. Gilmer has located at Hickory for practice.

Dr. F. T. Bower and Dr. Carlton Temple, Hattiesburg, have moved into new offices in the Hardy Street Medical Clinic.

The Central Medical Society has elected the following officers for the coming year: Dr. E. L. Green, Carpenter, President; Dr. T. E. Wilson, Jackson, Hinds County, Dr. J. W. Melvin, Camden, Madison County, Dr. H. N. Holyfield, Brandon, Rankin County, Dr. Austin, Scott County, Dr. A. E. Kennedy, Magee, Simpson County, and Dr. W. D. McCalip, Yazoo City, Yazoo County, Vice-Presidents.

The Pike County Medical Society has elected the following officers for the coming year: Dr. T. E. Hewitt, Summit, President; Dr. M. D. Ratcliff, McComb, Vice-President; and Dr. T. Paul Haney, Jr., McComb, Secretary-Treasurer.

The Tri-County Medical Society has elected the following officers for the coming year: Dr. C. L. Simmons, Hazlehurst, President; Dr. J. H. Beavers, Wesson, Copiah County, Dr. J. R. Markette, Brookhaven, Lincoln County, Dr. T. F. Conn, Monticello, Lawrence County, Dr. B. L. Crawford, Tylertown, Walthall County, Vice-Presidents; and Dr. H. R. Fairfax, Brookhaven, reelected Secretary-Treasurer.

Dr. F. T. Bower, Hattiesburg, and Miss Hazel Draughn were married recently.

Dr. Richard A. Street, Jr., Vicksburg, and Miss Catherine Noble were married recently.

Dr. Gilruth Darrington, Yazoo City, and Miss Anne Dubussion Hogue were married recently.

Dr. Kutcher Threefoot Klein and Mrs. Iva W. Lovell, both of Meridian, were married recently.

Deaths

Dr. Edmond D. Barron, Pattison, aged 69, died November 29 of carcinoma of the stomach and chronic myocarditis.

Dr. M. J. Lowry, Meridian, aged 76, died December 20.

MISSOURI

Dr. Logan Clendening, Kansas City, was a guest speaker on the program of the Academy of Medicine of Cleveland, Ohio, at their annual meeting recently.

Dr. Max A. Goldstein, St. Louis, was a guest speaker recently before the faculty and students of the University of Iowa School of Medicine.

The Adair County Medical Society has elected the following officers for the coming year: Dr. Spencer Freeman, Kirksville, President; Dr. George E. Grim, Kirksville, Vice-President; and Dr. J. S. Gashwiler, Novinger, Secretary-Treasurer.

The Buchanan County Medical Society has elected the following officers for the coming year: Dr. William C. Proud, President; Dr. Paul Forgrave, Vice-President; Dr. Emmett F. Cook, Secretary; and Dr. John M. Bell, Treasurer; all of St. Joseph.

The Gasconade-Maries-Osage County Medical Society has elected the following officers for the coming year: Dr. J. O. Cooper, Linn, President; Dr. John H. W. Baehr, Hermann, Vice-President; and Dr. O. H. Jones, Vienna, Secretary.

The Greene County Medical Society has elected the following officers for the coming year: Dr. Guy D. Callaway, President; Dr. Wallis Smith, Vice-President; Dr. John W. Williams, Jr., Secretary; and Dr. W. E. Handley, reelected Treasurer; all of Springfield.

The Marion-Ralls County Medical Society has elected the following officers for the coming year: Dr. F. E. Sultzman, Hannibal, President; Dr. W. D. Pipkin, Monroe, Vice-President; and Dr. W. F. Lauten, Hannibal, Secretary-Treasurer.

The Pettis County Medical Society has elected the following officers for the coming year: Dr. Cord Bohling, President; Dr. W. T. Bishop, Vice-President; Dr. J. B. Carlisle, Secretary; and Dr. A. E. Monroe, Treasurer; all of Sedalia.

Deaths

Dr. James E. Trexler, Kansas City, aged 59, died November 23 of injuries received in an automobile accident.

Dr. Bruno Louis Sulzbacher, Kansas City, aged 59, died November 14 of a fractured skull.

Dr. Phreeborn Grundy Paugh, St. Louis, aged 62, died November 24 of heart disease.

Dr. Benjamin H. Kirk, Union Star, aged 91, died November 20 of pulmonary emphysema.

Dr. Albert Habermaas, St. Louis, aged 61, died November 20 of cerebral hemorrhage.

Dr. James B. McPike, Smileyville, aged 76, died suddenly November 19.

Dr. Ola Putman, Marceline, aged 55, died December 4 of coronary thrombosis.

Dr. William Harrison, Marshall, aged 83, died September 18.

Dr. Reinhart L. Hild, St. Louis, aged 65, died November 19 of myocarditis and coronary thrombosis.

Dr. Bloom Warren Ganoung, St. Louis, aged 74, died suddenly November 9 of heart disease.

Dr. Joseph Ambrose Kerrigan, Webster Groves, aged 66, died November 5 of heart disease.

Dr. Stephen Allen Newman, Mount Vernon, aged 65, died August 18 of injuries received in an automobile accident.

Dr. Arthur J. Simpson, Chillicothe, aged 59, died October 31 of heart disease following pneumonia.

Dr. James Ashby Franklin, Cameron, aged 71, died November 10 of heart disease.

Dr. Claude H. McMahan, St. Louis, aged 58, died November 2 of injuries received in an automobile accident.

Continued on page 32

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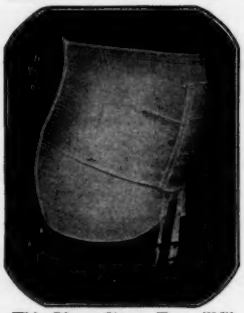

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(Krauss, W. E.: Bimonthly Bulletin, Ohio Agricultural Experiment Station, Ohio, U. S. A., Vol. XVIII, No. 164, Sept.-Oct., 1933)

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Continued from page 30

NORTH CAROLINA

Dr. Paul F. Whitaker, Kinston, was elected President of the Seaboard Medical Association of Virginia and North Carolina at its recent meeting held in Norfolk, Virginia. Dr. H. W. Carter and Dr. John Cotton Tayloe, both of Washington, were elected Vice-Presidents.

Following are the new officers for the coming year of the North Carolina State Board of Health: Dr. Carl V. Reynolds, Asheville, President; Dr. Sylvester D. Craig, Winston-Salem, Vice-President; and Dr. James M. Parrott, Raleigh, reelected Secretary.

The Mecklenburg County Medical Society has elected the following officers for the coming year: Dr. John Stuart Gaul, President; Dr. Sylvia Allen, First Vice-President; Dr. H. P. Barret, Second Vice-President; and Dr. R. D. McKnight, reelected Secretary-Treasurer; all of Charlotte.

Dr. J. Shelton Horsley, Richmond, Virginia, recently gave a clinic on Lesions of the Stomach and Colon at Duke Hospital, Durham.

Dr. Douglas Heath Nisbet, Charlotte, and Mrs. Pauline Hood Bowers were married in December.

Dr. Claude Henry Fryar, Oak Ridge, and Miss Lucie Sutton Hayes were married recently.

Dr. Cloyce R. Tew, Raleigh, and Miss Anna Rebekah Waaser were married recently.

Dr. Thomas H. Tomlinson, Thomasville, and Miss Mary Sweeney were married recently.

Dr. George Glasgow Chiles, Sanford, and Miss Mae McCleur Gilmore were married recently.

Dr. Douglas Hamilton Sprunt, Durham, and Miss Edith Charlescraft Lucas were married recently.

DEATHS

Dr. William Calvin Steele, Mount Olive, aged 66, died November 14 of cerebral hemorrhage.

Dr. Norman C. Hunter, Laurinburg, aged 58, died November 16.

Dr. John C. Twitty, Rutherfordton, aged 64, died November 6.

Dr. Samuel Harley Lyle, Franklin, aged 72, died November 14 of heart disease.

Dr. Thomas Marshall Sloan, Newton, aged 30, died November 12 of injuries received in an automobile accident.

OKLAHOMA

Dr. A. J. Weedn, Duncan, was recently reelected President of the Oklahoma State Hospital Association.

Dr. J. C. Hawkins, Blackwell, has been appointed temporarily to replace Dr. A. R. Havens as City Physician, and Dr. R. L. Edmonds, Blackwell, has been appointed Assistant City Physician.

Dr. Walter Hardy, Ardmore, has returned home from attending the Mayo Clinic at Rochester, Minnesota.

Dr. George L. Driver, Ponca City, has been in Kansas City taking special medical work.

Dr. Howard B. Alspaugh has located at Duncan, coming from Fort Worth, Texas.

DEATHS

Dr. Ralph Evans Runkle, Oklahoma City, aged 55, died November 23 of bronchopneumonia.

Dr. David Autrey, Marietta, aged 66, died November 21 of heart disease.

SOUTH CAROLINA

The Greenville County Medical Society has elected the following officers for the coming year: Dr. W. S. Judy, President; Dr. Jack Parker, Vice-President; Dr. W. McNeil Carpenter, Secretary; and Dr. J. W. Jervey, Jr., reelected Treasurer; all of Greenville.

Dr. Carl Caughman Sox, Columbia, and Miss Alluwee Babb were married recently.

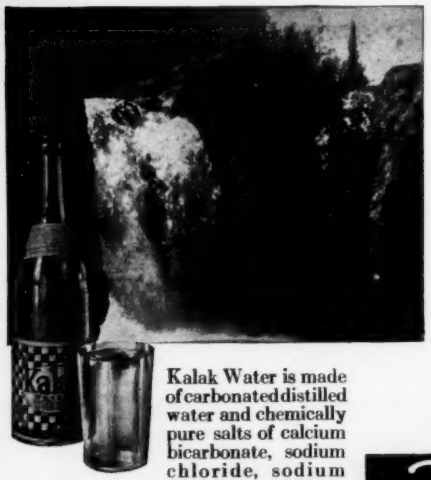
DEATHS

Dr. William David Senn, Newberry, aged 74, died suddenly November 23 of heart disease.

Dr. Rolfe Eldridge Hughes, Laurens, aged 65, died December 2.

Continued on page 34

A Pure, Palatable, Carbonated



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Kalak Water is made of carbonated distilled water and chemically pure salts of calcium bicarbonate, sodium chloride, sodium phosphate and bicarbonates of magnesium, potassium and sodium.

Kalak

Klim message of the month

Your Own Klim Formula Or A "Celluloid Feeding Chart"

When you tell a mother about WHOLE, POWDERED MILK (KLIM) you also give directions as to what must be added to this milk in order to meet the requirements of her baby *at that time.* To insure the best results from feeding babies, they must be under your supervision and changes in the formula must be made from time to time in order to meet the changing needs. When a baby is "put" on a "fixed" food and a feeding card accompanies the product the baby ceases to be an individual and becomes an "average" — in many instances he "gets along" because of the wide limits of his tolerance, but *he does not make optimum progress.*

AUTHORITY: "The prescribing of prepared infant foods has just about slipped out of the hands of the physician . . . The very presence of the samples of infant food seems to be a challenge to change the baby's food. It is easy to hand the mother a sample. And not a few mothers have the celluloid "feeding" card intended for the physician, to run their own show. The pediatricians are not responsible for this because they do not hand out samples."

(Dwyer, H. L., *South. Med. Jour.*, Vol., XXVI, No. 12, Dec., 1933)

PRESCRIBE

SAFE, PURE WHOLE MILK IN POWDERED FORM . . .

NRA MEMBER U.S. WE DO OUR PART

KLIM

ACCEPTED AMERICAN MEDICAL ASSN. Committee on Foods

Literature and samples sent on request

THE BORDEN COMPANY, DEPT. KM131, 205 E. 42ND ST., NEW YORK, N. Y.

Continued from page 32

TENNESSEE

The Middle Tennessee Medical Society held its seventy-eighth semi-annual meeting in Murfreesboro recently and elected the following officers for the coming year: Dr. R. B. Gaston, Lebanon, President; Dr. Theodore Morford, Nashville, Vice-President; and Dr. D. W. Smith, Nashville, Secretary-Treasurer.

The Hamilton County Medical Society has elected the following officers for the coming year: Dr. Franklin B. Bogart, President; Dr. James L. Bibb, Vice-President; and Dr. William J. Sheridan, Secretary-Treasurer; all of Chattanooga.

The Obion County Medical Society has elected the following officers for the coming year: Dr. W. B. Harrison, President; Dr. Ilar Glover, Union City, Vice-President; and Dr. Frank Kimzey, Union City, Secretary-Treasurer.

The Polk County Medical Society has elected the following officers for the coming year: Dr. H. P. Hyde, Copperhill, President; Dr. T. J. Hicks, Copperhill, Vice-President; and Dr. F. O. Geisler, Isabella, Secretary-Treasurer.

The Sullivan, Johnson Counties Medical Society has elected the following officers for the coming year: Dr. W. K. Vance, Bristol, President; Dr. J. V. Hodge, Kingsport, Vice-President from Sullivan County; Dr. J. C. Hutchinson, Crandull, Vice-President from Johnson County; and Dr. Arthur Hooks, Bristol, Secretary-Treasurer.

Dr. Robert E. Sullivan, Nashville, has moved into new offices in the Doctors Building.

Dr. Joseph McCrary, Bold Spring, and Mrs. Azalee Reynolds were married in December.

DEATHS

Dr. A. P. Massengill, Halls, aged 61, died November 29 of heart disease.

Dr. James K. Barlow, Savannah, aged 82; died November 11.

Dr. William C. Bilbro, Nashville, aged 70, died November 28.

Dr. James Brew, Nashville, aged 61, died November 25 of heart disease.

Dr. William Augustus Carnes, Memphis, aged 61, died November 20 of arteriosclerosis and bronchopneumonia.

Dr. John Quincy Owsley, Nashville, aged 62, died November 20 of carcinoma of the pancreas.

Dr. Samuel Edward Caldwell, Milan, aged 71, died November 15 of pneumonia.

TEXAS

The Texas Neurological Society met in Galveston at the State Psychopathic Hospital recently for its semi-annual session.

The Texas Pediatric Society met in San Antonio recently for its fall session.

Dr. R. E. Cogswell, Dimmitt, is taking postgraduate work in the Graduate School of Medicine, Tulane University, New Orleans.

Physicians of Hardin and Tyler Counties recently met and organized the Hardin-Tyler Counties Medical Society and elected the following officers for the coming year: Dr. J. H. Dameron, Silsbee, President; Dr. J. F. Shivers, Woodville, Vice-President; and Dr. John H. Hunter, Honey Island, Secretary-Treasurer.

The Lamb-Bailey-Hockley-Cochran Counties Medical Society has elected the following officers for the coming year: Dr. R. J. Sparks, Olton, President; Dr. H. N. Lusk, Levelland, Dr. A. R. Matthews, Muleshoe, Dr. D. T. Jordan, Morton, Vice-Presidents; and Dr. J. G. Little, Littlefield, Secretary-Treasurer.

The Limestone County Medical Society has elected the following officers for the coming year: Dr. J. F. Moore, Cooledge, President; Dr. J. W. Cox, Groesbeck, Vice-President; and Dr. O. T. Christoffer, Mexia, Secretary-Treasurer.

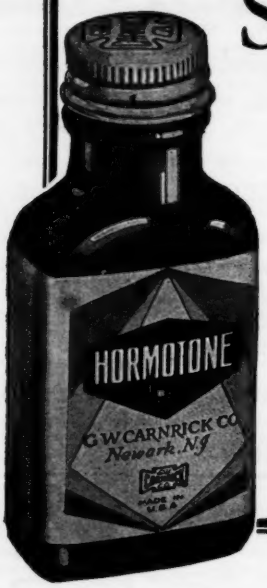
The Mid-West Texas (Second) District Medical Society held its annual session at Sweetwater recently and elected the following officers for the coming year: Dr. A. A. Chapman, Sweetwater, President; Dr. R. O. Peters, Sweetwater, Vice-President; and Dr. J. T. Bynum, Hamlin, Secretary-Treasurer.

The Red River County Medical Society has elected the following officers for the coming year: Dr. H. R. Smith, Detroit, President; Dr. William Henry Grayson, Bogata, Vice-President; and Dr. Gavin Watson, Clarksville, Secretary-Treasurer.

At a recent meeting of the Shelby County Medical Society it was decided to reorganize on a multiple county basis, and a new organization, the Shelby-San Augustine-Sabine Counties Medical Society was formed, with the following officers elected for the coming year: Dr. J. H. Windham, Shelbyville, President; Dr. W. T. Arnold, Hemphill, Vice-President; and Dr. W. H. Warren, Center, Secretary-Treasurer.

The Tierra-Blanco County Medical Society, composed of the counties of Randall, Deaf Smith, Parmer, Castro and Oldham,

Continued on page 36



SCANTY, painful or irregular menstruation usually results in fixed, faulty physiological habits. Treatment is more successful if instituted early.

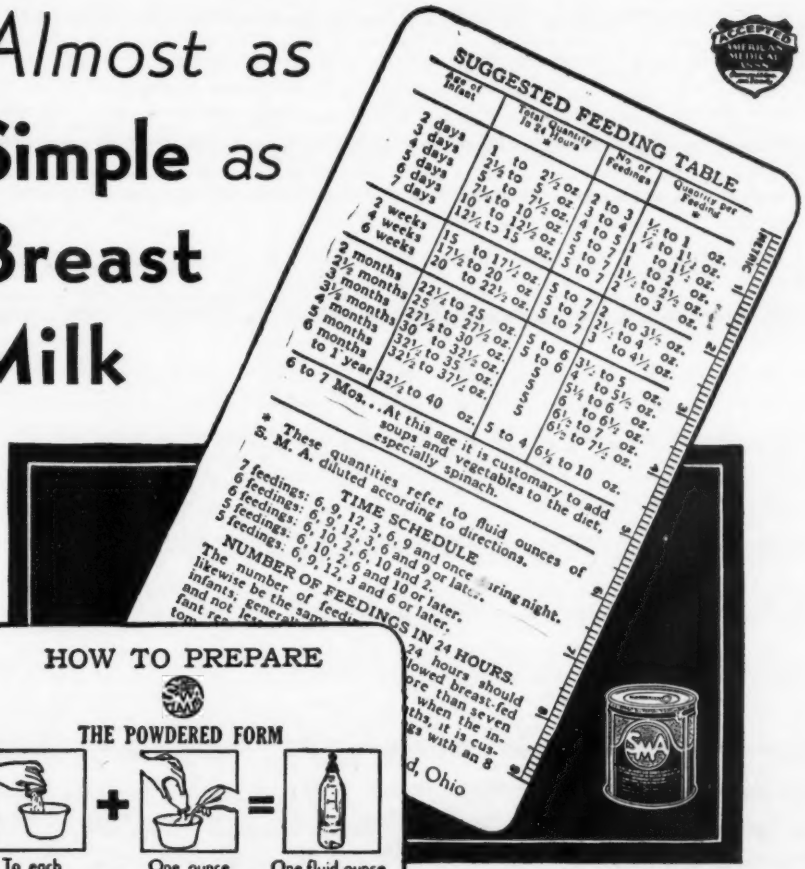
Take advantage of an endocrine product which represents the best thought of research and clinical medicine.

HORMOTONE

BOTTLES OF 50 and 100 TABLETS

G. W. Carnrick Co. 20 Mt. Pleasant Ave. Newark, N. J.

Almost as **Simple** *as* **Breast Milk**


ACCEPTED
AMERICAN MEDICAL ASSOCIATION
SUGGESTED FEEDING TABLE
Age of Infant
Total Quantity in 24 Hours *
No. of Feedings
Quantity per Feeding *
2 days
3 days
4 days
5 days
6 days
7 days
1 to 2½ oz.
2½ to 5 oz.
5 to 7½ oz.
7½ to 10 oz.
10 to 12½ oz.
12½ to 15 oz.
2 to 3
3 to 4
4 to 5
5 to 7
5 to 7
5 to 7
½ to 1 oz.
1 to 1½ oz.
1½ to 2 oz.
2 to 2½ oz.
2½ to 3 oz.
2 weeks
4 weeks
6 weeks
15 to 17½ oz.
17½ to 20 oz.
20 to 22½ oz.
5 to 7
5 to 7
5 to 7
2 to 3½ oz.
2½ to 4 oz.
3 to 4½ oz.
2 months
2½ months
3 months
3½ months
4 months
5 months
6 months
to 1 year
22½ to 25 oz.
25 to 27½ oz.
27½ to 30 oz.
30 to 32½ oz.
32½ to 35 oz.
32½ to 37½ oz.
32½ to 40 oz.
5 to 6
5 to 6
5
5
5
5
5 to 4
3½ to 5 oz.
5½ to 6 oz.
6 to 6½ oz.
6½ to 7 oz.
6½ to 7½ oz.
6½ to 10 oz.
6 to 7 Mos. . . At this age it is customary to add soups and vegetables to the diet, especially spinach.
* These quantities refer to fluid ounces of S. M. A. diluted according to directions.
TIME SCHEDULE
7 feedings: 6, 9, 12, 3, 6, 9 and once during night.
6 feedings: 6, 9, 12, 3, 6 and 9 or later.
6 feedings: 6, 10, 2, 6, 10 and 2.
5 feedings: 6, 10, 2, 6 and 10 or later.
5 feedings: 6, 10, 2, 6 and 10 or later.
NUMBER OF FEEDINGS IN 24 HOURS
The number of feedings in 24 hours should likewise be the same as followed breast-fed infants, generally speaking, and not more than seven
and not less than
SMA

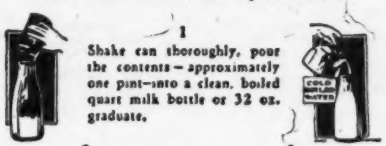
HOW TO PREPARE

THE POWDERED FORM

To each measure of S. M. A. — ADD — One ounce of boiled water → One fluid ounce of S. M. A. ready to feed.

To prepare a two ounce feeding, fill the cup twice and add two ounces of warm boiled water One fluid ounce S M A diluted according to directions is equivalent to 20 calories

THE CONCENTRATED LIQUID FORM



1 — Shake can thoroughly, pour the contents — approximately one pint—into a clean, boiled quart milk bottle or 32 oz. graduate.

2 — Fill the bottle to the top of the graduate to the 32 ounce mark with cold boiled water, and mix well.

3 — Divide the quart of prepared S M A into as many nursing bottles as the infant requires feedings and keep on ice or in a cool place.

NO ADDITIONAL COD LIVER OIL IS NECESSARY

It is NOT necessary to give cod liver oil with S M A as it contains an adequate amount to prevent rickets and spasmophilia

The kind of food constituents and their correlation in S M A also play a role in the prevention of rickets and spasmophilia

(ORANGE JUICE of course should be given the infant fed on S M A., just as it is the present practice to give it to breast fed infants.)

NO complicated feeding calculators are necessary in feeding S. M. A., the anti-rachitic breast milk adaptation.

As with breast milk, the total quantity of S. M. A. is merely increased as the infant's requirements increase with age.

For the convenience of the busy physician we have prepared the simple suggested feeding table shown above. On the other side are brief directions for the preparation of S. M. A. and suggestions on the amounts to be fed.

FREE: Send the coupon for your copy of this single thickness celluloid card, 2⅝" x 4⅛", with rounded corners to go into the pocket readily.

S. M. A. Corporation
4614 Prospect Avenue, Cleveland, Ohio
Please send me without charge or obligation

- ☐ Celluloid feeding card
- ☐ Trial Supply of S. M. A.
- ☐ Fourth revised edition of Milk Allergy booklet.

Attach coupon to your Rx blank or letterhead 12-24

Continued from page 34

was organized recently and the following officers elected for the coming year: Dr. C. E. Donnell, Canyon, President; Dr. D. K. Robison, Hereford, Vice-President; and Dr. T. L. Morgan, Hereford, Secretary-Treasurer.

The Texas Homeopathic Medical Association met in Dallas recently and elected the following officers for the coming year: Dr. Jesse L. Givens, Bowie, President; Dr. C. C. Bowes, Greenville, First Vice-President; Dr. Hunter B. Stiles, Waco, Second Vice-President; and Dr. M. L. Smith, Denison, Secretary-Treasurer.

The Medical and Surgical Association of the Southwest met in El Paso in December.

The Texas Public Health Association met in Mineral Wells recently for its annual session and elected the following officers for the coming year: Dr. T. J. McCamant, El Paso, President; Dr. E. F. Yeager, Mineral Wells, First Vice-President; Dr. J. H. Page, Houston, Second Vice-President; Dr. Jack Wyatt, Amarillo, Third Vice-President; Mrs. Zula Powell, Fort Worth, Fourth Vice-President; and Mrs. M. Pierson, Austin, reelected Secretary-Treasurer.

Deaths

Dr. Benjamin Oran Works, Brownsville, aged 51, died December 16 of heart disease.

Dr. George Washington Graves, Brownsfield, aged 61, died November 18 of coronary thrombosis.

Dr. Otto C. Jackson, Brady, aged 65, died November 30 of coronary occlusion.

Dr. Matthew D. Fullingim, Denton, aged 60, died suddenly October 16 of heart disease.

Dr. Lamartine O. Dudgeon, Sweetwater, aged 57, died October 1.

Dr. James Madison Bannister, Snyder, aged 54, died October 12 of heart disease.

Dr. Marquis Ernest Gilmore, Fort Worth, aged 63, died December 2 in an automobile accident.

Dr. William Harry Tatman, Bellaire, aged 64, died September 19.

Dr. Walter D. Cross, Corsicana, aged 66, died November 8 of coronary occlusion and arteriosclerosis.

Dr. Theodore E. Bryant, Houston, aged 58, died August 25 of cerebral hemorrhage.

Dr. Robert James Prather, Dallas, died in November of cerebral hemorrhage.

Dr. J. F. Hendricks, Merkel, aged 79, died October 27 of senility.

The "MESCO" Laboratories manufacture the largest line of Ointments in the world. Sixty different kinds. We are originators of the Professional Package. Specify "MESCO" when prescribing ointments. Send for lists.

Manhattan Eye Salve Co.

LOUISVILLE, KENTUCKY

Classified Advertisements

FOR SALE—Office furniture, apparatus and medical library of the late Dr. I. B. May. Communicate with Miss Irby L. May, Columbia, Louisiana.

ASSISTANCE OFFERED TO MEDICAL WRITERS. Research. Abstracts. Translations (all languages). Papers prepared from author's data. Ten years' experience with leading physicians and appointments on medical journals of highest standing. I employ no assistants; all my work is done personally and is reliable. Florence Annan Carpenter, 413 St. James Place, Chicago, Ill.

Dr. John W. Palmer, Knippa, aged 78, died October 31 of tuberculosis.

Dr. Frank B. Bryan, Childress, aged 53, died October 20.

VIRGINIA

The Richmond Academy of Medicine, at its first meeting in December, elected the following officers for the coming year: Dr. Joseph F. Geisinger, President; Dr. F. P. Fletcher and Dr. A. I. Dodson, Vice-Presidents; and Dr. T. D. Jones, Acting Secretary; all of Richmond.

Dr. Stuart McGuire, Richmond, was recently elected President of the Association of Surgeons of the C. and O. Railway; Dr. J. M. Emmett, Clifton Forge, was elected Vice-President; and Mr. G. E. Meanley, Richmond, reelected Secretary.

Dr. J. E. Hamner, formerly of Rainelle, West Virginia, is taking a residency in ear, nose and throat at Memorial Hospital, Richmond.

The Seaboard Medical Association of Virginia and North Carolina met in Norfolk recently for its annual session and elected the following officers for the coming year: Dr. Paul F. Whitaker, Kinston, North Carolina, President; Dr. C. J. Andrews, Norfolk, Dr. H. W. Carter, Washington, North Carolina, Dr. C. J. Riddick, Suffolk, Dr. John Cotton Tayloe, Washington, North Carolina, Vice-Presidents; Dr. A. M. Burfoot, Fentress, Treasurer; and Dr. Clarence Porter Jones, Newport News, Secretary.

The Lynchburg Academy of Medicine has elected the following officers for the coming year: Dr. R. D. Caldwell, President; Dr. W. Clyde Adkerson, Vice-President; and Dr. John Hundley, Jr., Secretary-Treasurer; all of Lynchburg.

The Petersburg Medical Faculty has elected the following officers for the coming year: Dr. William B. McIlwaine, President; Dr. C. S. Dodd, Dr. Leta J. White, Vice-Presidents; and Dr. W. M. Bowman, reelected Secretary-Treasurer.

The Southside Virginia Medical Association has elected the following officers for the coming year: Dr. Herbert C. Jones, Petersburg, President; Dr. S. E. Gunn, Hopewell, Dr. John A. Proffitt, Burkeville, Dr. M. H. Todd, Norfolk, Dr. C. V. Montgomery, South Hill, Vice-Presidents; and Dr. R. L. Raiford, Franklin, Secretary-Treasurer.

The Southern Surgical Association held its annual meeting in Hot Springs recently and elected the following officers for the coming year: Dr. Frank K. Boland, Atlanta, Georgia, President; Dr. J. H. Neff, University, Virginia, Dr. E. P. Hogan, Birmingham, Alabama, Vice-Presidents; and Dr. R. L. Payne, Norfolk, Virginia, reelected Secretary-Treasurer.

The Warwick County Medical Society has elected the following officers for the coming year: Dr. F. W. Poindexter, President; Dr. G. G. Hankins, Vice-President; and Dr. B. L. Carleton, Secretary-Treasurer; all of Newport News.

Dr. J. Shelton Horsley, Richmond, presented a clinic at the Duke Hospital, Durham, North Carolina, in December.

Dr. William Ambrose McGee and Miss Lois Imogene Lacy, both of Richmond, were married in December.

Dr. John Randolph Perdue, Jr., Rocky Mount, and Miss Jean Barksdale Jones were married in December.

The Medical College of Virginia, Richmond, observed Founders' Day in December, celebrating the ninety-sixth session of the College.

Deaths

Dr. Leon O. Vaughan, Waverly, aged 57, died November 26 of heart disease.

Dr. Zeb Vance Sherrill, Marion, aged 71, died December 11 in a Richmond hospital.

WEST VIRGINIA

Dr. J. M. Moore, formerly of Charleston, has moved to Logan, where he has become associated with the Staff of the Hatfield-Lawson Hospital as House Physician.

Dr. Walter W. Brewer, Logan, has opened a new hospital, the Logan Clinic, and has associated with him Dr. C. L. Border as first assistant and House Physician.

The Association of Surgeons of the C. and O. Railway held its annual meeting in White Sulphur Springs recently.

The Central West Virginia Medical Society has elected the following officers for the coming year: Dr. L. W. Deeds, Buckhannon, President; Dr. Clayton C. Carson, Gassaway, Vice-President; and Dr. Eugene Brown, Summersville, Secretary-Treasurer.

Dr. Samuel Basil Souleyret, Coalburg, and Miss Goldie Elizabeth Knight were married recently.

Deaths

Dr. Andrew Blair Nelson, Eastbank, aged 52, died September 18 of heart disease.

Dr. Wilson I. Gautier, Athens, aged 72, died August 10 of nephritis.

MISINFORMATION BUREAU

Pseudo-facts fly thick and fast when the go-cart brigade assembles in the park . . .

Soon Mrs. Neighbor gets going full tilt on her favorite theories of infant feeding, and —well, it's just one more time when a baby's best friend is his doctor! For only a physician's advice—plus his explicit formula—can protect a youngster from haphazard, park-bench prescriptions.

For example . . . you know that certain brands of evaporated milk measure up to your high standards, while others may not. But unless you have told the mother specifically what brand of evaporated milk to use, Mrs. Neighbor's careless counsel may prevail. And your little patient may be given a milk that would never meet with your approval.

Borden's Evaporated Milk fulfills the strictest medical requirements for infant feeding. The raw milk is carefully chosen. And every step in its preparation is rigidly supervised under constant laboratory control.

May we send you a simple, compact infant feeding formulary—and other literature which you will, we believe, also find helpful? Address The Borden Company, Dept. SN24, 350 Madison Avenue, New York.

Borden's Evaporated Milk was the first evaporated milk for infant feeding to be submitted to the American Medical Association Committee on Foods, and the first to receive the seal of acceptance.

ACCEPTED AMERICAN MEDICAL ASSN. Committee on Foods

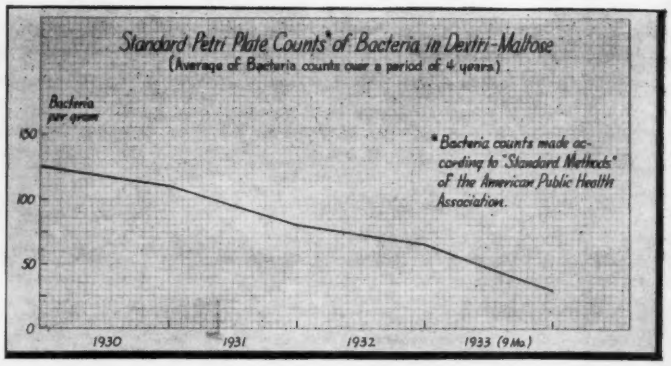
Borden's

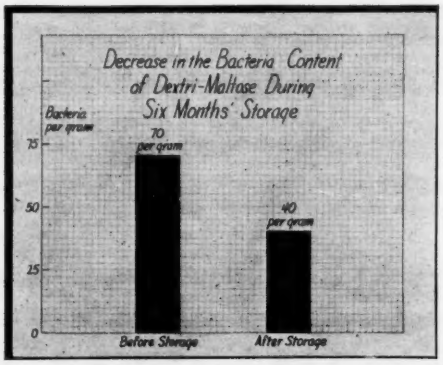
EVAPORATED MILK

Why we supply DEXTRI-MALTOSE in Powder form only . . .

It is mechanically and bacteriologically clean

Prepared in powdered form, Dextri-Maltose is not likely to form a culture medium for micro-organisms. This graph shows that the bacteria count during a 4-year period is well under 125 per gram and only 30 in recent analyses. Contrast this with the count of 10,000 per cc., the maximum allowable for certified milk.



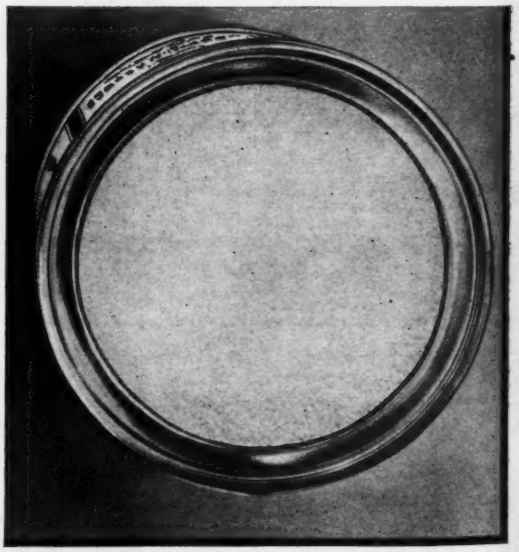


Its bacteria count decreases during storage

A representative sample of Dextri-Maltose which, to start had a low bacteria count of 70 per gram, revealed a count of only 40 per gram after standing for 6 months at room temperature. During this period the container was opened 12 times for biweekly sampling, without any special precautions being taken to prevent contamination. Yet the bacteria count actually decreased.

It will not support bacterial growth even after inoculation

The tin of Dextri-Maltose shown at right was inoculated with the thrush organism, a common dust-borne fungus. At the end of 17 days the Dextri-Maltose was free from visible growth. This is explainable by the fact that bacteria, yeasts, and fungi require moisture for reproduction—and the moisture content of Dextri-Maltose is extremely low, only 5 per cent. It is safe to say that no baby can be infected with thrush or other organisms from Dextri-Maltose, *per se*.



DEXTRI-MALTOSE
clean — not cleaned

Please enclose professional card when requesting samples to prevent their reaching unauthorized persons. Mead Johnson & Co., Evansville, Ind.

"We will specify Mead's Capsules of Viosterol in Halibut Liver Oil 250 D when Mead puts them on the market"

— many physicians told us.

so now—by request we offer CAPSULES

MEAD'S VIOSTEROL IN HALIBUT LIVER OIL 250 D
Each 3-minim capsule supplies not less than 5,500 U.S.P. Vitamin A units and 570 Steenbock Vitamin D units.

WHEN recommending Mead's Capsules, the physician is now assured of the same high grade product which is marketed by Mead in liquid form, and he also knows that Mead's Capsules are not advertised to the public.

Furthermore, the physician who prefers his patients to have these capsules with a prescription label and without a trade name will be interested in the special Mead dispensing package containing 4 plain unlabelled boxes of 25 capsules each, to which the druggist's own label can be affixed. This obviates the need for the druggist either to paste his prescription label over a trade package or to rehandle the capsules in transferring them to his own capsule container which may or may not be of suitable size, shape, and capacity.

"The fish's name is HALIBUT"— Specify MEAD'S

THE NEAT TIN BOX

contains 25 Mead Capsules and assures maximum protection in all climates and seasons to both capsules and clothing. No additional charge for this convenient fine package. Specify MEAD'S— not advertised to the public.

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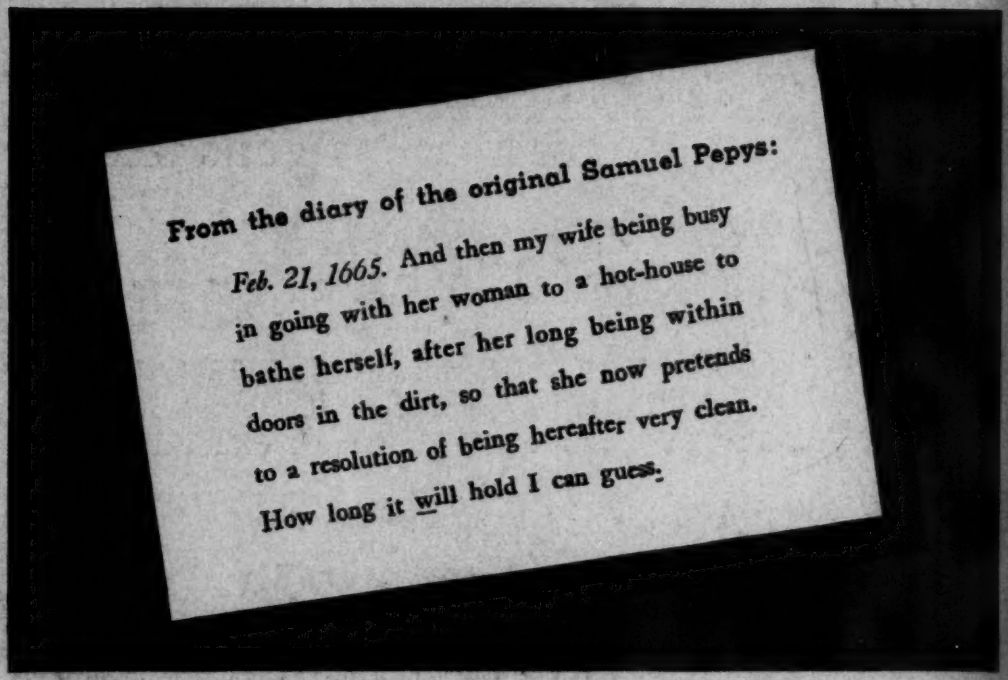
From the diary of the original Samuel Pepys:
Feb. 21, 1665. And then my wife being busy in going with her woman to a hot-house to bathe herself, after her long being within doors in the dirt, so that she now pretends to a resolution of being hereafter very clean. How long it will hold I can guess.

An apology for Mrs. Samuel Pepys

MRS. PEPYS did not take many baths—but no one did in the 17th Century.

Cold houses, lack of even tub-and-sponge facilities, made bathing an ordeal. The desirability of cleanliness was recognized, as Pepys' comment indicates—but the *practice* of cleanliness did not begin until bathing was made *pleasanter.*

Parke-Davis has applied much the same reasoning to vitamin therapy—*i. e.*, by making vitamin therapy pleasanter, its field can be substantially broadened. And to make it pleasanter, you have Parke-Davis Haliver Oil products.

It is a well-known fact that adults are more squeamish than children about taking cod-liver oil, and preparations containing it. Their aversion to fish oil is completely obviated by the high potency of Haliver Oil. All the adult patient has to do is to take one or two tiny, tasteless capsules, instead of those distasteful teaspoonfuls.

When vitamins A and D are needed, prescribe Parke-Davis Haliver Oil. Because it's pleasanter, you'll have the satisfaction of knowing that your treatment is being followed. And this holds true for children as well as adults.

Parke-Davis Haliver Oil (either Plain or with Viosterol-250 D and in bottle or capsule form) is available at practically all drug stores in the United States and Canada.

HALIVER OIL WITH VIOSTEROL-250 D
Containing 32,000 vitamin A units (U. S. P. X.) and 3,333 vitamin D units (Steenbock) per gram.

HALIVER OIL PLAIN
32,000 vitamin A units (U. S. P. X.) and 200 vitamin D units (Steenbock) per gram.

●

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The World's Largest Makers of Pharmaceutical and Biological Products